PESTICIDAL SUBSTITUTED 1,2,5-THIADIAZOLE DERIVATIVES

This application claims the benefit of U.S. Provisional Application No. 60/485,297, filed July 7, 2003.

FIELD OF THE INVENTION

The present invention relates to methods for controlling pests. In particular, it relates to control by the application of certain novel compositions containing pesticidal substituted 1,2,5-thiadiazole derivatives.

BACKGROUND OF THE INVENTION

It is well known that pests such as insects and acarids can cause significant damage, not only to crops grown in agriculture, but also, for example, to structures and turf where the damage is caused by soil-borne insects, such as termites and white grubs. Such damage may result in the loss of millions of dollars of value associated with a given crop, turf or structure. Insecticides and acaricides are useful for controlling insects and acarids which may otherwise cause significant damage to crops such as wheat, corn, soybeans, potatoes, and cotton to name a few. For crop protection, insecticides and acaricides are desired which can control the insects and acarids without damaging the crops, and which have no deleterious effects to mammals and other living organisms. Surprisingly, it has now been found that compositions of substituted 1,2,5-thiadiazole derivatives of the present invention are unexpectedly active in controlling acarids, for example two-spotted spider mites; and also in controlling insects such as cotton aphids and termites, as well as other insect species.

Pharmacologically active 1,2,4-, 1,3,4-, and 1,2,5-oxadiazoles and 1,2,4-, 1,3,4-and 1,2,5-thiadiazoles have been reported in the literature, for example, Wätjen et al., U.S. Patent No. 4,870,073; Baker et al., U.S. Patent Nos. 4,952,587 and 5,686,463 and European Patent EP 0323864 A2; Sauerberg et al., U.S. Patent Nos. 5,260,314, 5,481,240 and 5,527,813; Sauerberg et al., Journal of Medicinal Chem., Vol. 35, No. 12, pp. 2274-2283 (1992); Olesen et al., Eur. J. Med. Chem., 31, pp. 221-230 (1996); and MacLeod et al., Journal of Medicinal Chem., Vol. 33, pp. 2052-2059 (1990). Similarly, insecticidally and acaricidally active 1,2,4-, 1,3,4-, and

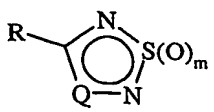
1,2,5-oxadiazoles, 1,2,3-, 1,2,4- and 1,3,4-thiadiazoles, 1,2,4-triazoles, and 1,2,3,4-tetrazoles have been reported in the literature. For example, Dick, U.S. Patent No. 5,393,767; Tsubata et al., U.S. Patent Nos. 6,337,341 B1 and 6,348,460 B1; Theobald et al., U.S. Patent No. 4,943,584; and Matsumoto et al., U.S. Patent No. 4,722,934. EP 0445731 A1 and WO 01/15532 disclose azabicyclo and azacyclo oxime and amine compounds as pesticides. It has also been disclosed that pharmacologically active 1,2,4- and 1,2,5-thiadiazoles and insecticidally and acaricidally active 1,2,4-oxdiazoles, 1,3,4-triazoles, and 1,2,3,4-tetrazoles can act as muscarinic agonists, see, for example, Sauerberg et al., Journal of Medicinal Chem., Vol. 35, No. 12, pp. 2274-2283 (1992); Dick et al., Pestic. Sci., 49, 268-276 (1997); Olesen et al., Eur. J. Med. Chem., 31, pp. 221-230 (1996); and MacLeod et al., Journal of Medicinal Chem., Vol. 33, pp. 2052-2059 (1990).

WO 95/03306 discloses arthropodically active substituted 1,2,5-oxadiazoles and 1,2,5-thiadiazoles; however, it specifically requires that the 1,2,5-oxadiazole or 1,2,5-thiadiazole be substituted with an azabicyclic compound rather than a tetrahydropyridyl or a pyridyl ring and that said azabicyclic compound can only attach at the two position when the bridge occurs between the nitrogen and a carbon atom on the ring.

WO 93/14636 and its equivalent U.S. Patent No. 5,244,906 disclose certain substituted 1,2,4-oxadiazoles and 1,2,4-thiadiazoles useful for control of insects, such as sucking insects like two-spotted spider mite.

SUMMARY OF THE INVENTION

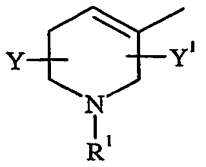
It has now been found that certain compositions containing an effective amount of a 1,2,5-thiadiazole derivative, and their agriculturally acceptable salts, in admixture with at least one agriculturally acceptable extender or adjuvant are surprisingly effective in controlling sucking pests, i.e., acaricides, as well as insects. The 1,2,5-thiadiazole derivatives may be represented by the following formula I:



I

where

-R is an azacycle selected from:



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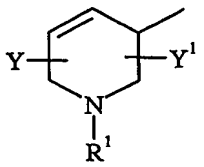

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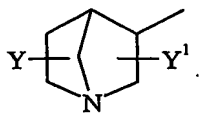

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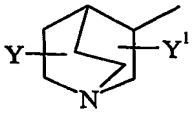

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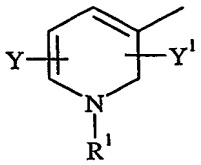

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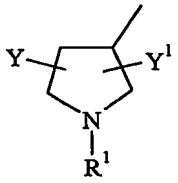

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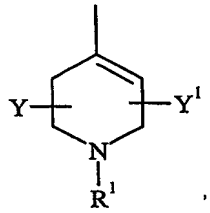

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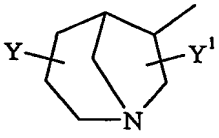

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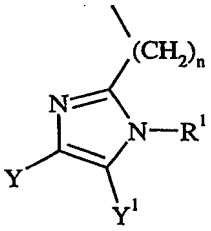

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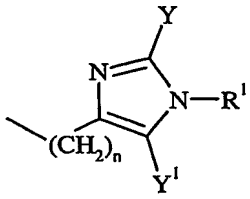

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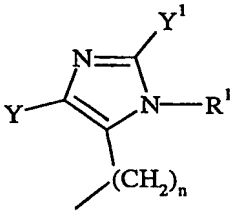

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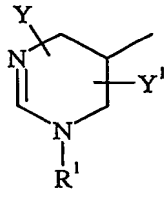

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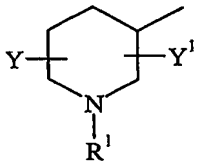

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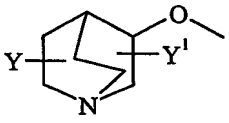

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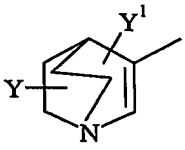

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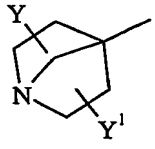

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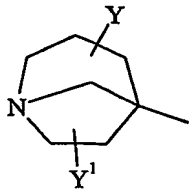

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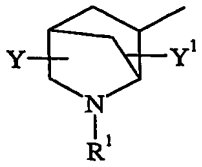

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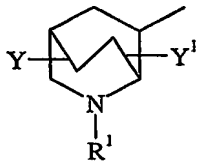

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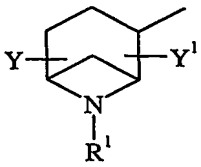

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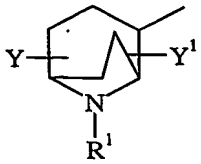

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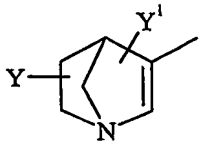

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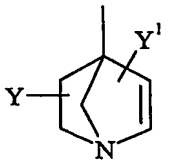

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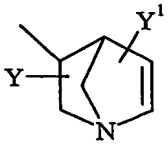

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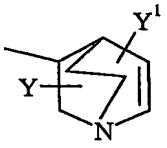

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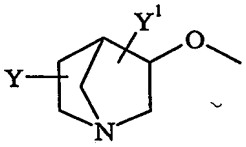

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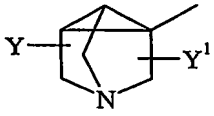

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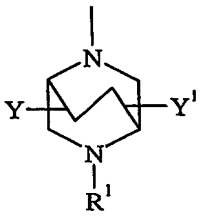

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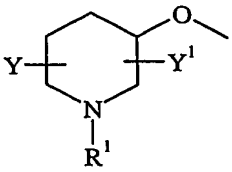


W29

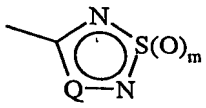
where

-Y and Y^1 may be attached at the same or different positions, and are independently selected from hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkenyl, alkoxy, haloalkoxy, aminoalkoxy, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, arylalkyl, aryl, aryloxy, and heterocyclyl, where the aryl and heterocyclyl moieties may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, or haloalkoxy;

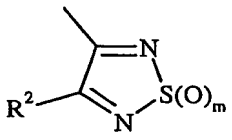
n is an integer from 0 to 2;

R^1 is selected from hydrogen, alkyl, haloalkyl, alkenyl, haloalkenyl, alkenyloxy, alkynyl, alkynyloxy, alkoxy, alkoxyalkyl, haloalkoxy, alkylcarbonyl, alkyloxycarbonyl, alkoxycarbonylalkoxy, arylcarbonyl, aryloxycarbonyl, haloalkoxycarbonyl, carboxyl and arylalkyl; wherein the aryl may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, or haloalkoxy;

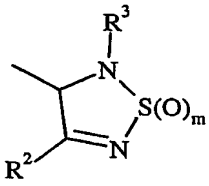
and wherein



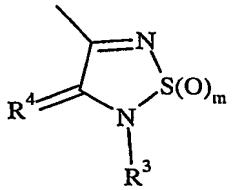
is a 1,2,5-thiadiazole where Q is CR^2 or $C=R^4$, wherein said 1,2,5-thiadiazole is selected from



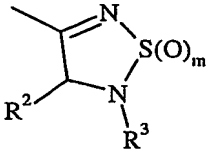
Ia
a 1,2,5-thiadiazol-3-yl



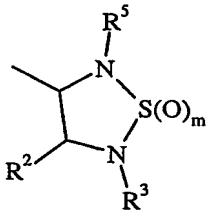
Ib
a 1,2,5-thiadiazolin-3-yl



Ic
a 1,2,5-thiadiazolin-3-R^4-4-yl



Id
a 1,2,5-thiadiazolin-4-yl



Ie
a 1,2,5-thiadiazolidin-3-yl

where

m is an integer from 0 to 2;

$-R^2$ is selected from hydrogen, hydroxy, halogen, amino, nitro, alkyl, haloalkyl, alkenyl, haloalkenyl, alkynyl, haloalkynyl, alkylaryl, alkoxy, haloalkoxy, aryloxy, alkenyloxy, haloalkenyloxy, alkynyloxy; thiol, alkylthio, haloalkylthio, cyanoalkylthio, arylthio, alkenylthio, alkynylthio, alkyloxycarbonyl, carboxyl; $-N(R^6)(R^7)$; $-NHN(R^6)(R^7)$; $-NHC(O)R^6$; $-NHC(O)OR^6$; $-OC(O)R^6$;

where the aryl may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, cyano, or haloalkoxy moiety;

where

R^6 and R^7 are independently selected from hydrogen, alkyl, arylalkyl, alkoxy, acetyl, alkoxycarbonyl, alkoxyalkyl, aminoalkyl, and carbonylamino;

$-R^3$ and R^5 are independently selected from hydrogen, hydroxy, alkyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, $-N(R^8)(R^9)$; $-NHC(O)R^8$ and $-NHC(O)OR^8$; where the aryl may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, cyano, or haloalkoxy moiety;

where

R^8 and R^9 are independently selected from hydrogen, alkyl, arylalkyl, alkoxy, acetyl, alkoxycarbonyl, alkoxyalkyl, aminoalkyl, and aminocarbonyl; or are taken together with R^1 to form a hetero-atom link;

$-R^4$ is selected from O, S and NR^{10};

where

R^{10} is selected from hydrogen, alkyl, alkoxy, alkoxyalkyl, alkenyl, alkynyl, alkenyloxy, alkynyloxy, aryl and arylalkyl;

and

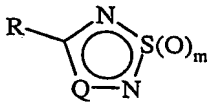
the corresponding agriculturally acceptable salts thereof.

The present invention also relates to a method of controlling insects and acarids that comprises applying an insecticidally or acaricidally effective amount of the above composition to a locus of crops, such as cotton, vegetables or fruits, where control of insects and/or acarids is desired.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to compositions containing a pesticidally effective amount of a substituted 1,2,5-thiadiazole derivative or their agriculturally acceptable salts, in admixture with at least one agriculturally acceptable extender or adjuvant. These compositions are surprisingly effective as pesticides, i.e., as acaricides and insecticides. The 1,2,5-thiadiazole derivatives useful in the

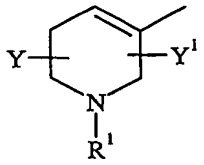
compositions of the present invention may be represented by the following formula I:



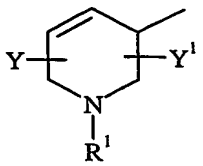
I

where

-R is an azacycle selected from:



W1



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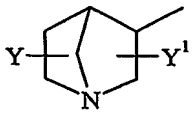

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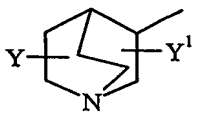

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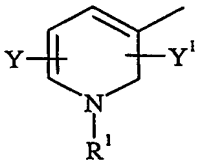
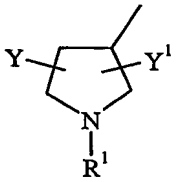


W5



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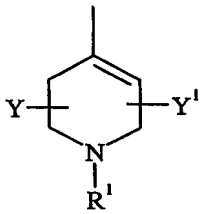

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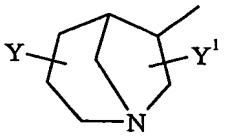

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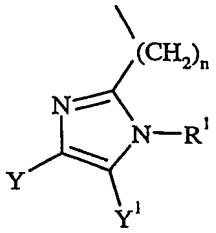

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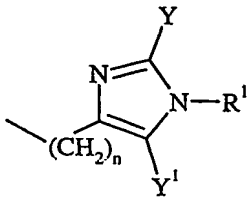

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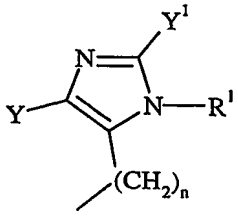

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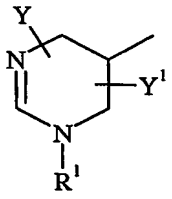

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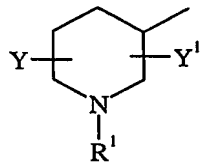

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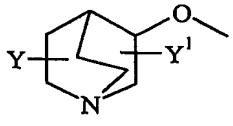

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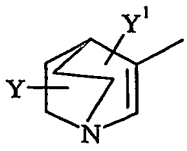

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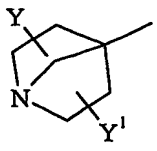

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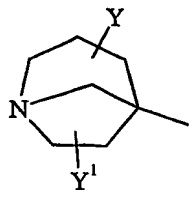

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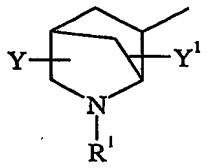

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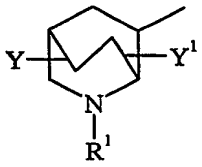

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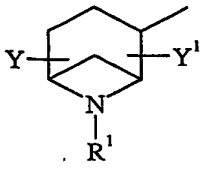

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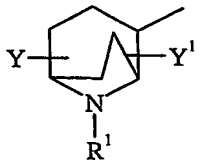

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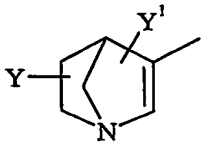

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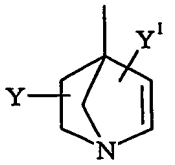

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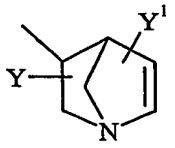

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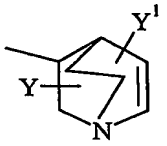

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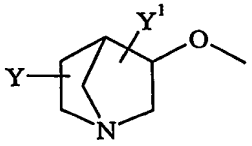

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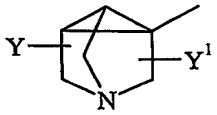

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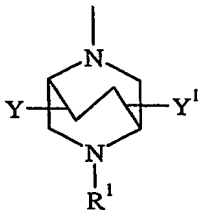

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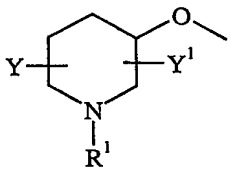


W29

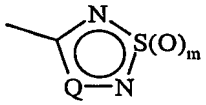
where

-Y and Y^1 may be attached at the same or different positions, and are independently selected from hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkenyl, alkoxy, haloalkoxy, aminoalkoxy, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, arylalkyl, aryl, aryloxy, and heterocyclyl, where the aryl and heterocyclyl moieties may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, or haloalkoxy;

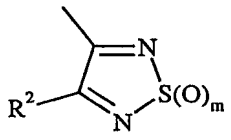
n is an integer from 0 to 2;

R^1 is selected from hydrogen, alkyl, haloalkyl, alkenyl, haloalkenyl, hydroxyalkenyloxy, alkynyl, alkynyloxy, alkoxy, alkoxyalkyl, haloalkoxy, alkylcarbonyl, alkyloxycarbonyl, alkoxycarbonylalkoxy, arylcarbonyl, aryloxycarbonyl, haloalkoxycarbonyl, carboxyl and arylalkyl; wherein the aryl may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, or haloalkoxy;

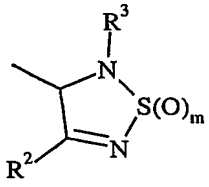
and wherein



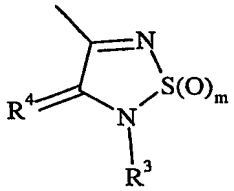
is a 1,2,5-thiadiazole where Q is CR^2 or $C=R^4$, wherein said 1,2,5-thiadiazole is selected from



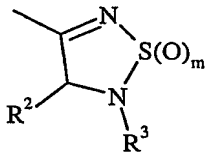
Ia
a 1,2,5-thiadiazol-3-yl



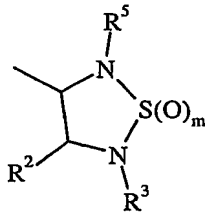
Ib
a 1,2,5-thiadiazolin-3-yl



Ic
a 1,2,5-thiadiazolin-3-R^4-4-yl



Id
a 1,2,5-thiadiazolin-4-yl



Ie
a 1,2,5-thiadiazolidin-3-yl

where

m is an integer from 0 to 2;

$-R^2$ is selected from hydrogen, hydroxy, halogen, amino, nitro, alkyl, haloalkyl, alkenyl, haloalkenyl, alkynyl, haloalkynyl, alkylaryl, alkoxy, haloalkoxy, aryloxy, alkenyloxy, haloalkenyloxy, alkynyloxy; thiol, alkylthio, haloalkylthio, cyanoalkylthio, arylthio, alkenylthio, alkynylthio, alkyloxycarbonyl, carboxyl; $-N(R^6)(R^7)$; $-NHN(R^6)(R^7)$; $-NHC(O)R^6$; $-NHC(O)OR^6$; $-OC(O)R^6$;

where the aryl may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, cyano, or haloalkoxy moiety;

where

R^6 and R^7 are independently selected from hydrogen, alkyl, arylalkyl, alkoxy, acetyl, alkoxycarbonyl, alkoxyalkyl, aminoalkyl, and carbonylamino;

$-R^3$ and R^5 are independently selected from hydrogen, hydroxy, alkyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, $-N(R^8)(R^9)$; $-NHC(O)R^8$ and $-NHC(O)OR^8$; where the aryl may be optionally substituted with halogen, alkyl, haloalkyl, alkoxy, cyano, or haloalkoxy moiety;

where

R^8 and R^9 are independently selected from hydrogen, alkyl, arylalkyl, alkoxy, acetyl, alkoxycarbonyl, alkoxyalkyl, aminoalkyl, and aminocarbonyl; or are taken together with R^1 to form a hetero-atom link;

$-R^4$ is selected from O, S and NR^{10};

where

R^{10} is selected from hydrogen, alkyl, alkoxy, alkoxyalkyl, alkenyl, alkynyl, alkenyloxy, alkynyloxy, aryl and arylalkyl;

and

the corresponding agriculturally acceptable salts thereof.

According to nomenclature used to name organic molecules, those moieties designated as Ia-Ie above are not always named as 1,2,5-thiadiazoles. Moieties Ib-Id are often named as 1,2,5-thiadiazolines, whereas moiety Ie may be named as a 1,2,5-thiadiazolidine. For purposes of the present invention, moieties Ia-Ie are all referred to as "1,2,5-thiadiazoles" and derivatives thereof.

Agriculturally acceptable salts of the 1,2,5-thiadiazole derivatives of the present invention include, without limitation, iodide and bromide salts and the salts of hydrochloric acid, hydrobromic acid, hydroiodic acid, ethanesulfonic acid, trifluoroacetic acid, methylbenzenesulfonic acid, phosphoric acid, gluconic acid, pamoic acid, and carboxylic acid.

Preferred compositions comprised of the 1,2,5-thiadiazole derivatives of the present invention, selected from those set forth above, are those where the azacycle R is selected from W1, W3, W4, W8; W10 and W11, where n is 1 or 2; W13, W14, W15, W20, W26, W28 and W29;

where

-Y and Y^1 are independently selected from hydrogen and halogen;

-R^1 is selected from hydrogen, alkyl, haloalkyl, alkoxyalkyl, arylalkyl, alkenyl, haloalkenyl, alkynyl, alkylcarbonyl and alkoxycarbonyl;

and,

the 1,2,5-thiadiazole is selected from i) Ia, where m is 0, and ii) Ib and Id, where m is 0 or 2;

where

-R^2 is selected from hydrogen, halogen, alkoxy, alkenyloxy, alkynyloxy, alkylthio, alkenylthio, and alkynylthio;

and

-R^3 is selected from hydrogen, hydroxy, alkyl, alkoxyalkyl, aryl and $N(R^8)(R^9)$;

where

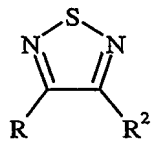
R^8 and R^9 are independently selected from hydrogen, alkyl, alkoxy and alkoxyalkyl.

More preferred compositions comprised of the 1,2,5-thiadiazole derivatives of the present invention, selected from those set forth above, are those where the azacycle R is selected from W1, W3, W4, W13, W14 and W26, where Y and Y^1 are hydrogen and R^1 is selected from hydrogen, alkyl, haloalkyl, alkoxyalkyl, alkylcarbonyl, alkoxycarbonyl and arylalkyl; and said 1,2,5-thiadiazole is selected from i) Ia, where m 0.

Yet more preferred compositions comprised of the 1,2,5-thiadiazole derivatives are those compositions where the azacycle R is selected from W1, W3 and W4; R^1 is selected from alkyl, haloalkyl, alkoxyalkyl and arylalkyl; and R^2 is selected from hydrogen, halogen, alkoxy, alkynyloxy and alkynylthio.

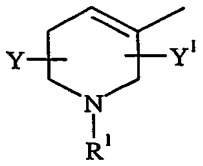
More specifically, compositions containing an insecticidally and acaricidally effective amount of a substituted 1,2,5-thiadiazole derivative and their agriculturally acceptable salts, in admixture with at least one agriculturally acceptable extender or

adjuvant are surprisingly effective as acaricides and insecticides. The 1,2,5-thiadiazole derivatives may be represented by the following formula I:

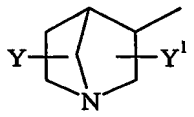


I

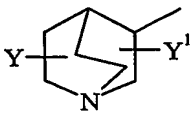
where R is an azacycle selected from the following:



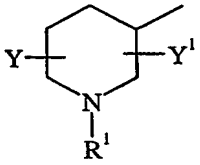
W1



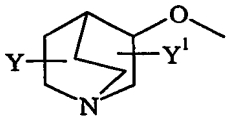
W3



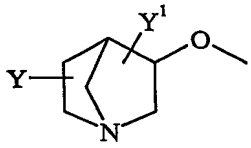
W4



W13



W14



W26

where

-Y and Y^1 are hydrogen;

R^1 is selected from hydrogen, alkyl, haloalkyl, alkoxyalkyl, alkylcarbonyl, alkoxycarbonyl and arylalkyl;

and

-R^2 is selected from hydrogen, halogen, alkoxy, alkenyloxy, alkynyloxy, alkylthio, alkenylthio, and alkynylthio.

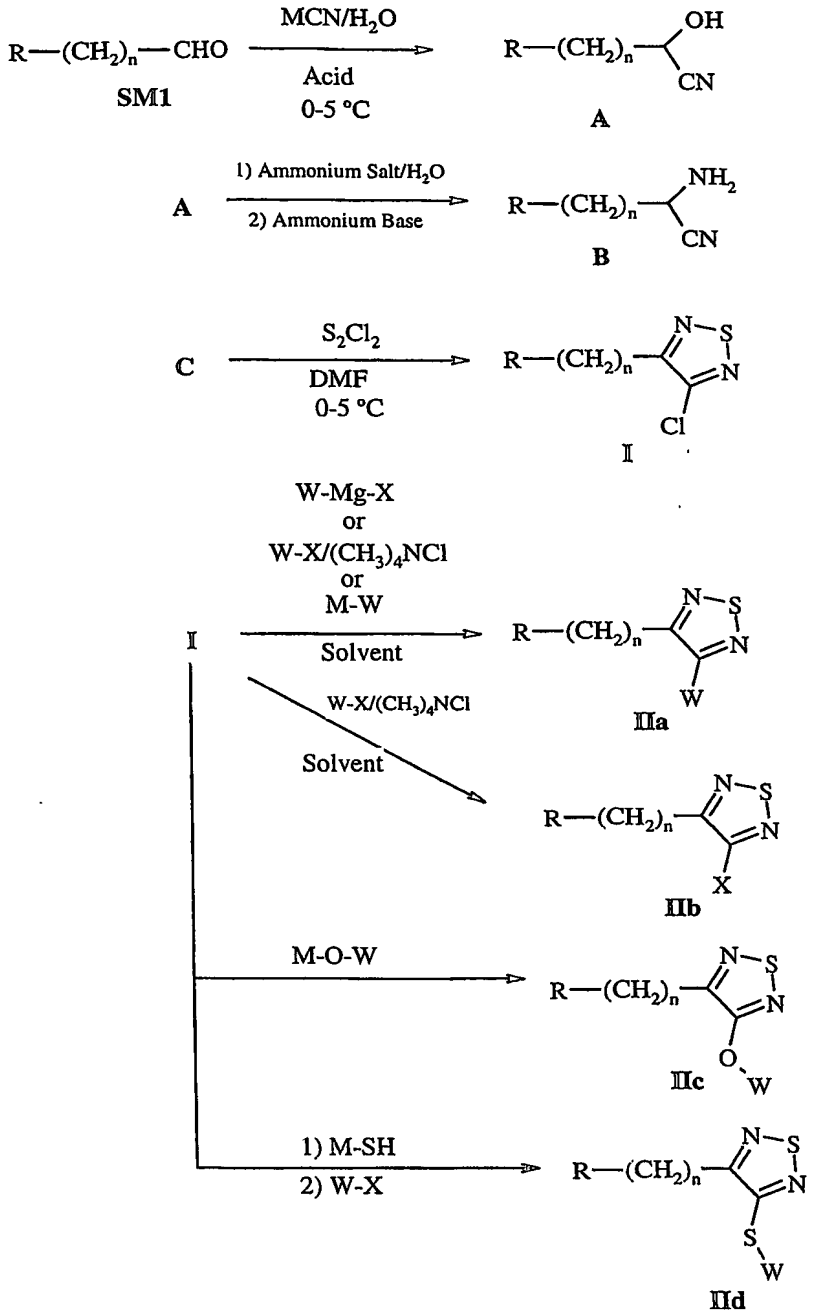
Preferred compositions comprised of the 1,2,5-thiadiazole derivatives of the present invention, selected from those set forth above, are those where the azacycle R is selected from W1, W3 and W4; R^1 is selected from hydrogen, alkyl, haloalkyl, alkoxyalkyl and arylalkyl; and R^2 is selected from hydrogen, halogen, alkoxy, alkynyloxy and alkynylthio; more preferably where R^1 is selected from hydrogen and alkyl, and R^2 is selected from hydrogen, chlorine, fluorine, alkoxy and alkynyloxy.

As used in this specification and unless otherwise indicated, the substituent terms "alkyl" and "alkoxy", alone or as part of a larger moiety, include chains of 1 to 14 carbon atoms, preferably straight or branched alkyls of 1 to 6 carbon atoms; while "halogen" or "halo", alone or as part of a larger moiety, includes chlorine, bromine, fluorine, and iodine atoms. The terms "alkenyl" or "alkynyl", used alone or as part of a larger moiety, includes straight or branched chains of at least two carbon atoms containing at least one carbon-carbon double or triple bond, preferably up to 12 carbon atoms, more preferably, up to ten carbon atoms, most preferably up to seven carbon atoms. The term "cycloalkyl" includes rings of three to twelve carbon atoms, preferably rings of three to six carbon atoms. The terms "haloalkyl" and "haloalkoxy", alone or as part of a larger moiety, include straight or branched chain alkyls of 1 to 14 carbon atoms, preferably lower straight or branched chain alkyls of 1 to 6 carbon atoms, wherein one or more hydrogen atoms have been replaced with halogen atoms, as, for example, trifluoromethyl or 2,2,2-trifluoroethoxy, respectively. "Aryl" refers to an aromatic ring structure, including fused rings, having 5 to 10 carbon atoms. "Heterocyclyl" refers to an aromatic ring structure, including fused rings, having at least one nitrogen, sulfur or oxygen atom. "Amino" refers to compounds of nitrogen that may be considered derived from ammonia and includes primary, secondary and tertiary amines wherein one or more of the hydrogen atoms is replaced with alkyl groups. "THF" refers to tetrahydrofuran, "DMF" refers to N,N-dimethylformamide, "MeOH" refers to methanol, "EtOH" refers to ethanol, "DMAC" refers to N,N-dimethylacetamide, and "TEA" refers to triethylamine. The term 'pesticide" or 'pesticidal" refers to insecticide, acaricide or insecticidal and acaricidal, respectively. The term "pesticidally effective amount" refers to an insecticidally effective amount and an acaricidally effective amount, and as used in the context of the present invention, refers to a rate of application of a compound of the present invention applied to a locus where insect and acarid control is needed. Such a pesticidally effective amount in the context of the present invention is in the range of 10ppm to 1000ppm. Of course, one skilled in the art will realize that the pesticidally effective amount may not be the same to control both insects and acarids.

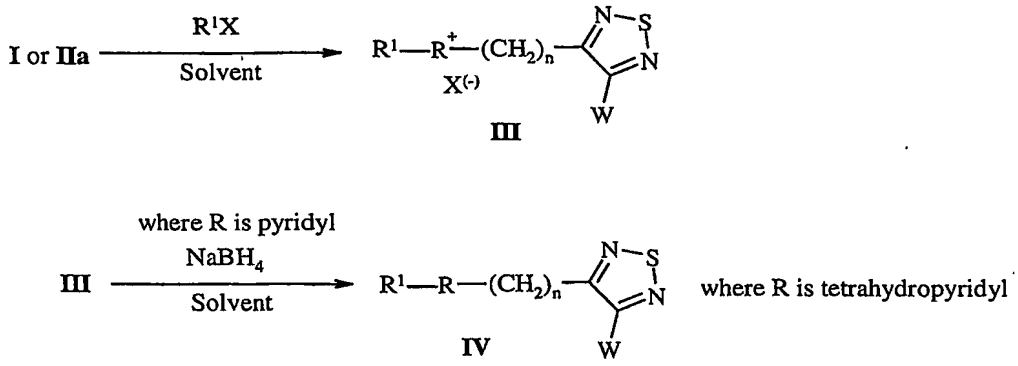
The compounds of the present invention may be synthesized by methods that are individually known to those skilled in the art from intermediate compounds readily available in commerce. Many of the compounds of the present invention in which R is an azabicyclyl are prepared in the manner shown in Schema 1, as set forth below:

Schema 1

Where R is an azacyclic moiety; M is sodium, potassium, cessium; X is halo; m is 0 or 1; n is 0-2



Schema 1 (continued)



As depicted in Schema 1, a substituted azacyclycarboxyaldehyde (**SM1**) is reacted with a cyanide complex, for example, potassium cyanide, in an acid, for example, acetic acid, at 0-5 °C to yield the appropriately substituted hydroxyazacyclylalkylnitrile (**A**). The appropriately substituted hydroxyazacyclylalkylnitrile (**A**) is then reacted with an ammonium salt, for example, ammonium chloride, in water followed by an ammonium base, for example ammonium hydroxide, to yield the appropriately substituted aminoazacyclylalkylnitrile (**B**). The appropriately substituted aminoazacyclylalkylnitrile (**B**) is then be reacted with sulfur monochloride in a solvent, for example, DMF or THF, at 0-5 °C to yield the targeted substituted 3-chloro-4-azacyclyl-1,2,5-thiadiazole (**I**), for example, 3-chloro-4-pyrid-3-yl-1,2,5-thiadiazole.

Appropriately substituted 1,2,5-thiadiazoles may be prepared from (**I**). The substituted 3-chloro-4-azacyclyl-1,2,5-thiadiazole (**I**) is then be reacted with: 1) the appropriately substituted magnesium halide, for example, methyl magnesium chloride, or the appropriately substitute metal complex in a solvent, for example, DMF or THF, to yield the targeted 3-substituted-4-azacyclyl-1,2,5-thiadiazole (**IIa**), for example –4-pyrid-3-yl-1,2,5-thiadiazole; 2) the appropriately substituted halide, for example, potassium fluoride, in the presence of tetramethylammonium chloride in a solvent, for example, DMF, to yield the targeted 3-substituted-4-azacyclyl-1,2,5-thiadiazole (**IIa**) or the targeted 3-halo-4-azacyclyl-1,2,5-thiadiazole (**IIb**), for example, 3-fluoro-4-azacyclyl-1,2,5-thiadiazole; 3) the appropriately substituted

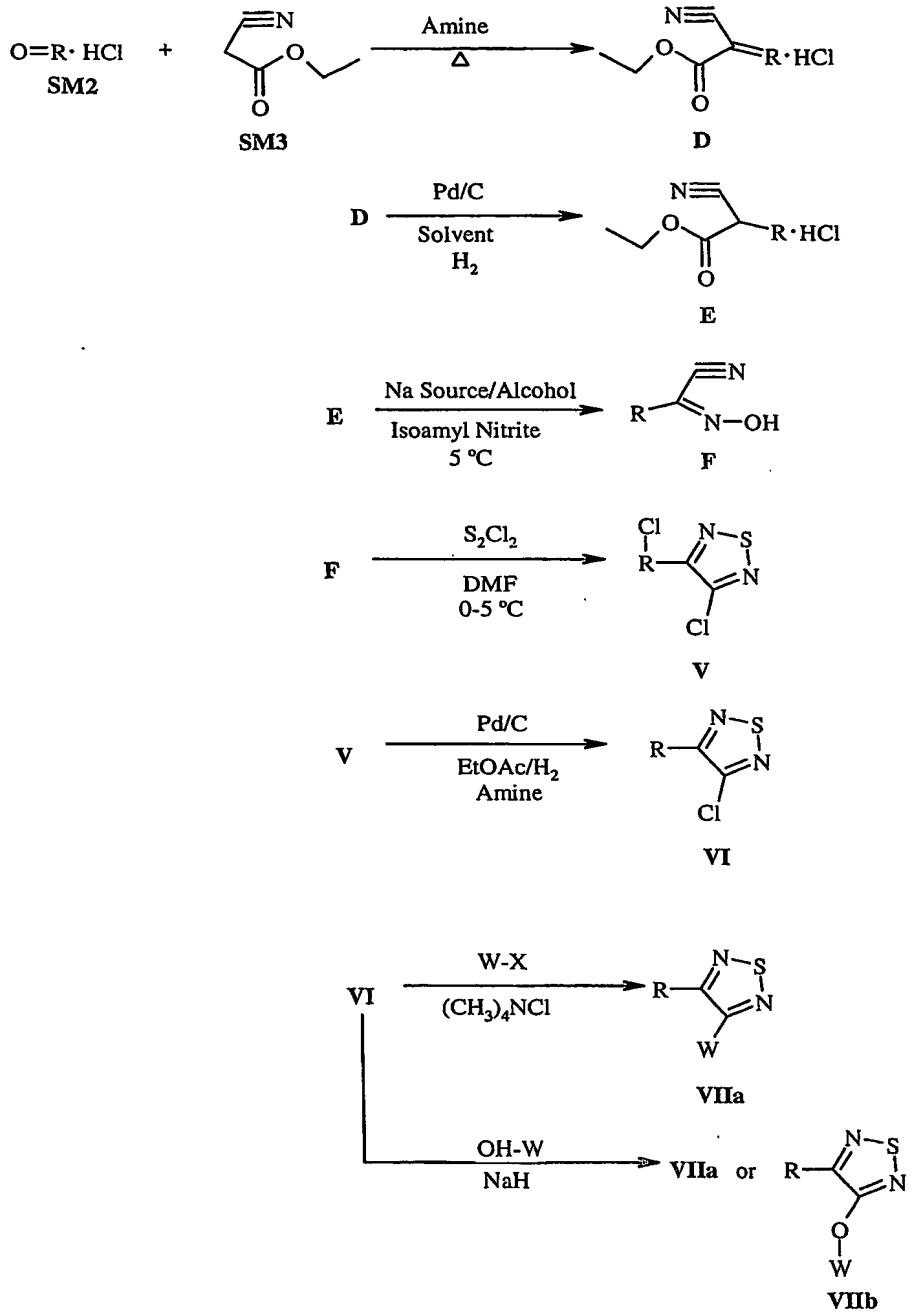
metal oxa complex to yield the targeted 3-substituted oxa-4-azacyclyl-1,2,5-thiadiazole (IIIc); a metal sulfur complex followed by the appropriately substituted halide to yield the targeted 3-substituted thio-4-azacyclyl-1,2,5-thiadiazole (IIId).

Agriculturally acceptable salts of the 1,2,5-thiadiazoles may be prepared by reacting the 3-chloro-4-azacyclyl-1,2,5-thiadiazole (II) or the 3-substituted-4-azacyclyl-1,2,5-thiadiazole (IIIa) with the appropriately substituted halide, for example, benzyl bromide or methyl iodide, to yield the targeted salt of the 3-substituted-4-azacyclyl-1,2,5-thiadiazole (III), for example, the bromide salt of 3-chloro-4-(1-benzylpyrid-3-yl)-1,2,5-thiadiazole or the iodide salt of 3-fluoro-4-(1-methylpyrid-3-yl)-1,2,5-thiadiazole. When the azacyclyl is a pyridyl, it may be reacted with sodium borohydride in a solvent, for example, THF, MeOH, or EtOH, to form the targeted 3-substituted-4-tetrahydropyridyl-1,2,5-thiadiazole (IV), for example, 3-chloro-4-[1-benzyl(1,2,5,6-tetrahydropyrid-3-yl)]-1,2,5-thiadiazole or 3-fluoro-4-(1-methyl-1,2,5,6-tetrahydropyrid-3-yl)-1,2,5-thiadiazole.

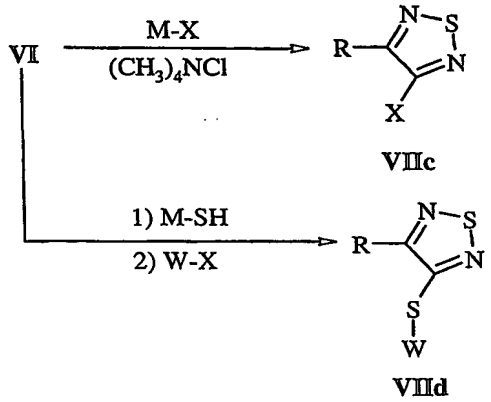
Compounds of the present invention in which R is a bridged azacyclyl are prepared in a manner shown in Schema 2, as set forth below:

Schema 2

Where R is a bridged azacyclic moiety; X is halo:



Schema 2 (continued)



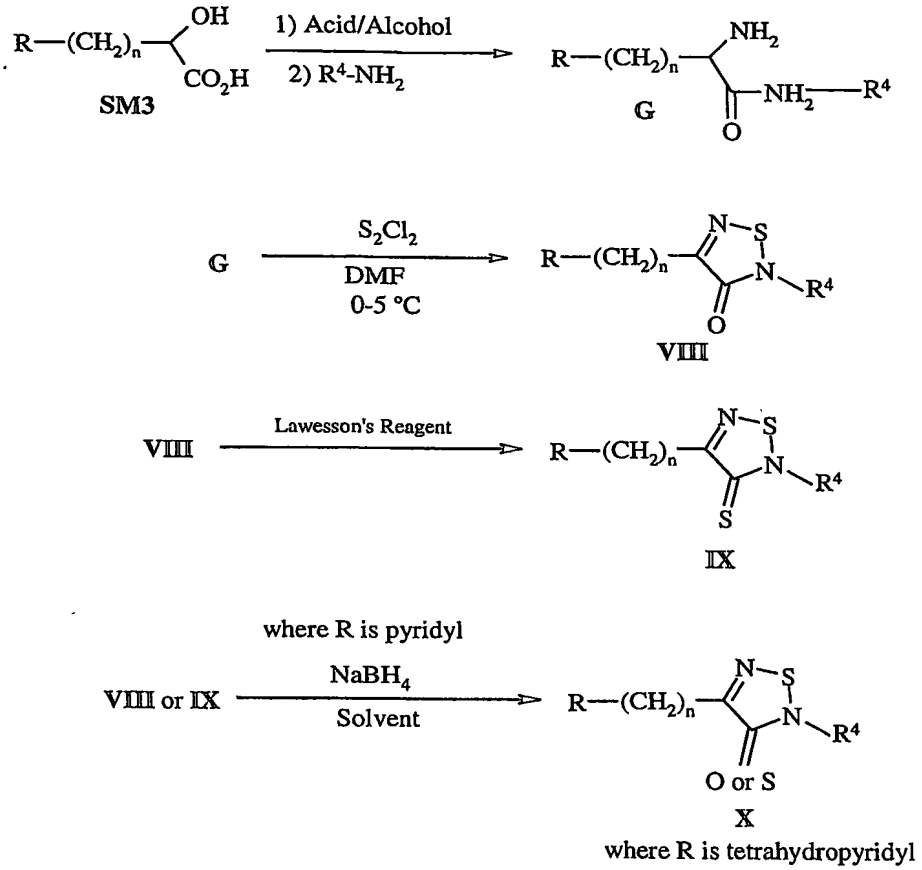
As depicted in Schema 2, compounds of the present invention wherein R is a bridged azacyclyl moiety are prepared by reacting the appropriately substituted oxo-containing bridged azacyclyl compound (SM2), for example, 3-quinuclidinone hydrochloride, with ethyl cyanoacetate (SM3) in the presence of an amine, for example, TEA, at elevated temperature to form the appropriately substituted ethyl 2-cyano-2-(bridged azacyclyl)-ylideneacetate hydrochloride (D). The appropriately substituted ethyl 2-cyano-2-(bridged azacyclyl)ylideneacetate hydrochloride (D) is then hydrogenated with palladium on carbon in a solvent, for example, EtOH or methylene chloride, to yield the appropriately substituted ethyl 2-cyano-2-(bridged azacyclyl)acetate hydrochloride (E), for example, ethyl 2-cyano-2-quinuclidin-3-ylacetate. The substituted ethyl 2-cyano-2-(bridged azacyclyl)acetate hydrochloride (E), is then reacted with a sodium source in the presence of isoamyl nitrite at 5 °C to yield the appropriately substituted 2-(hydroxyimino)-2-(bridged azacyclyl)ethanenitrile (F) which is then reacted with sulfur monochloride in DMF in the manner described above to yield the targeted 3-chloro-4-(chloro substituted bridged azacyclyl)-1,2,5-thiadiazole (V), for example, 3-chloro-4-(3-chloroquinuclidin-3-yl)-1,2,5-thiadiazole. The 3-chloro-4-(chloro substituted bridged azacyclyl)-1,2,5-thiadiazole (V) may then be hydrogenated with palladium on carbon in the presence of an amine in the manner described above to yield the targeted 3-chloro-4-(bridged azacyclyl)-1,2,5-thiadiazole (VI), for example, 3-chloro-4-quinuclidin-3-yl-1,2,5-thiadiazole.

Similar to above, appropriately substituted 1,2,5-thiadiazoles may be prepared (VI). The 3-chloro-4-(bridged azacyclyl)-1,2,5-thiadiazole (VI) may then be reacted with: 1) the appropriately substituted halide in the presence of tetramethylammonium chloride in the manner described above to yield the targeted 3-substituted-4-(bridged azacyclyl)-1,2,5-thiadiazole (VIIa) or the targeted 3-halo-4-(bridged azacyclyl)-1,2,5-thiadiazole (VIIc); 2) the appropriately substituted alochol, for example, n-butanol or ethanol, in the presence of sodium hydride to yield the targeted 3-substituted-4-(bridged azacyclyl)-1,2,5-thiadiazole (IIIa) or the targeted 3-subtituted oxy-4-(bridged azacyclyl)-1,2,5-thiadiazole (VIIb), for example, 3-butoxy-4-quinuclidin-3-yl-1,2,5-thiadiazole; or 3) a metal sulfur complex and appropriately substituted halide in the manner described above to yield the targeted 3-substituted thio-4-(bridged azacyclyl)-1,2,5-thiadiazole (VIId).

Compounds of the present invention, where for example, the five-membered heterocyclic portion of the molecule contains a ketone or thioketone moiety may be prepared by a method set forth in Schema 3 below:

Schema 3

Where R is an azacylic moiety; n is 0-2



As depicted in Schema 3, a substituted 2-amino-(2-azacyclylalkyl) acetic acid (SM3), for example, 2-amino-2-(3-pyridyl)acetic acid, is reacted with an acid, for example, hydrochloric acid, in an alcohol, for example, ethanol, followed by the appropriately substituted amine to yield the appropriately substituted 2-amino-(2-azacyclylalkyl)acetamide (G). The appropriately substituted 2-amino-(2-azacyclylalkyl)acetamide (G) is then reacted with sulfur monochloride in a solvent, for example, DMF or THF, in the manner described above to yield the targeted substituted 4-azacyclyl-1,2,5-thiadiazolin-3-one (VIII). The appropriately substituted 4-azacyclyl-1,2,5-thiadiazolin-3-one (VIII) is then reacted with Lawesson's Reagent to yield the target 4-azacyclyl-1,2,5-thiadiazolin-3-thione (IX).

When the azacyclyl moiety is a pyridyl, it may be reacted with sodium borohydride in a solvent, for example, THF, MeOH, or EtOH, in the manner described above to form the targeted 4-tetrahydropyridyl-1,2,5-thiadiazolin-3-one or 4-tetrahydropyridyl-1,2,5-thiadiazolin-3-thione (X).

The compositions of the present invention are those compositions that are normally employed in the art for facilitating the dispersion of active ingredients for the particular utility desired, recognizing the fact that the composition and mode of application of a toxicant may affect the activity of the material in a given application. Thus, for agricultural use the present insecticidal and acaricidal compositions may be granules of relatively large particle size, water-soluble or water-dispersible granules, powdery dusts, wettable powders, emulsifiable concentrates, solutions, or as any of several other known types of compositions, depending on the desired mode of application.

These insecticidal and acaricidal compositions may be applied either as water-diluted sprays, or dusts, or granules to the areas in which insect and arachnid control is desired. These compositions may contain as little as 0.1%, 0.2% or 0.5% to as much as 95% or more by weight of active ingredient.

Dusts are free flowing admixtures of the active ingredients with finely divided solids such as talc, natural clays, kieselguhr, flours such as walnut shell and cottonseed flours, and other organic and inorganic solids which act as dispersants and carriers for the toxicant; these finely divided solids have an average particle size of less than about 50 microns. A typical dust composition useful herein is one containing 1.0 part or less of the insecticidal and acaricidal compound and 99.0 parts of talc.

Wettable powders are in the form of finely divided particles which disperse readily in water or other dispersant. The wettable powder is ultimately applied to the locus where insect and arachnid control is desired either as a dry dust or as an emulsion in water or other liquid. Typical carriers for wettable powders include Fuller's earth, kaolin clays, silicas, and other highly absorbent, readily wet, inorganic diluents. Wettable powders normally are prepared to contain about 5-80% of active ingredient, depending on the absorbency of the carrier, and usually also contain a small amount of a wetting, dispersing, or emulsifying agent to facilitate dispersion.

For example, a useful wettable powder composition contains 80.8 parts of the insecticidal and acaricidal compound, 17.9 parts of Palmetto clay, and 1.0 part of sodium lignosulfonate and 0.3 part of sulfonated aliphatic polyester as wetting agents.

Other useful compositions for insecticidal and acaricidal applications are emulsifiable concentrates (ECs) which are homogeneous liquid compositions dispersible in water or other dispersant, and may consist entirely of the insecticidal and acaricidal compound and a liquid or solid emulsifying agent, or may also contain a liquid carrier, such as xylene, heavy aromatic naphthas, isophorone, or other non-volatile organic solvent. For insecticidal and acaricidal application these concentrates are dispersed in water or other liquid carrier, and normally applied as a spray to the area to be treated. The percentage by weight of the essential active ingredient may vary according to the manner in which the composition is to be applied, but in general comprises 0.5 to 95% of active ingredient by weight of the insecticidal and acaricidal composition.

Flowable compositions are similar to ECs except that the active ingredient is suspended in a liquid carrier, generally water. Flowables, like ECs, may include a small amount of a surfactant, and contain active ingredient in the range of 0.5 to 95%, frequently from 10 to 50%, by weight of the composition. For application, flowables may be diluted in water or other liquid vehicle, and are normally applied as a spray to the area to be treated.

Typical wetting, dispersing, or emulsifying agents used in agricultural compositions include, but are not limited to, the alkyl and alkylaryl sulfonates and sulfates and their sodium salts; alkylaryl polyether alcohols; sulfated higher alcohols; polyethylene oxides; sulfonated animal and vegetable oils; sulfonated petroleum oils; fatty acid esters of polyhydric alcohols and the ethylene oxide addition products of such esters; and the addition product of long-chain mercaptans and ethylene oxide. Many other types of useful surface-active agents are available in commerce. The surface-active agents, when used, normally comprise from 1 to 15% by weight of the composition.

Other useful compositions include suspensions of the active ingredient in a relatively non-volatile solvent such as water, corn oil, kerosene, propylene glycol, or other suitable solvents.

Still other useful compositions for insecticidal and acaricidal applications include simple solutions of the active ingredient in a solvent in which it is completely soluble at the desired concentration, such as acetone, alkylated naphthalenes, xylene, or other organic solvents. Granular compositions, wherein the toxicant is carried on relatively coarse particles, are of particular utility for aerial distribution or for penetration of cover crop canopy. Pressurized sprays, typically aerosols wherein the active ingredient is dispersed in finely divided form as a result of vaporization of a low boiling dispersant solvent carrier, such as carbon dioxide, propane, or butane, may also be used. Water-soluble or water-dispersible granules are also useful compositions for insecticidal and acaricidal application of the present compounds. Such granular compositions are free-flowing, non-dusty, and readily water-soluble or water-miscible. The soluble or dispersible granular compositions described in U.S. Pat. No. 3,920,442 are useful herein with the present insecticidal and acaricidal compounds. In use by the farmer on the field, the granular compositions, emulsifiable concentrates, flowable concentrates, solutions, etc., may be diluted with water to give a concentration of active ingredient in the range of say 0. 1% or 0.2% to 1.5% or 2%.

The active insecticidal compounds of this invention may be formulated and/or applied with one or more second compounds. Second compounds include, but are not limited to, other pesticides, plant growth regulators, fertilizers, soil conditioners, or other agricultural chemicals. In applying an active compound of this invention, whether formulated alone or with other agricultural chemicals, an effective amount and concentration of the active compound is of course employed; the amount may vary in the range of, e.g. about 0.02 to about 1.5kg/ha, preferably about 0.05 to about 0.3 kg/ha. For field use, where there are losses of insecticide, higher application rates (e.g., four times the rates mentioned above) may be employed.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such

as herbicides, the herbicides include, without limitation, for example: N-(phosphonomethyl)glycine ("glyphosate"); aryloxyalkanoic acids such as (2,4-dichlorophenoxy)acetic acid ("2,4-D"), (4-chloro-2-methylphenoxy)acetic acid ("MCPA"), (+/-)-2-(4chloro-2-methylphenoxy)propanoic acid ("MCPP"); ureas such as N,N-dimethyl-N'-[4-(1-methylethyl)phenyl]urea ("isoproturon"); imidazolinones such as 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-pyridinecarboxylic acid ("imazapyr"), a reaction product comprising (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-4-methylbenzoic acid and (+/-)2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-methylbenzoic acid ("imazamethabenz"), (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid ("imazethapyr"), and (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-quinolinecarboxylic acid ("imazaquin"); diphenyl ethers such as 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid ("acifluorfen"), methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate ("bifenox"), and 5-[2-chloro-4-(trifluoromethyl)phenoxy]-N-(methylsulfonyl)-2-nitrobenzamide ("fomasafen"); hydroxybenzonitriles such as 4-hydroxy-3,5-diiodobenzonitrile ("ioxynil") and 3,5-dibromo-4-hydroxybenzonitrile ("bromoxynil"); sulfonylureas such as 2-[[[[(4chloro-6-methoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]benzoic acid ("chlorimuron"), 2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide (achlorsulfuron"), 2-[[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sufonyl]methyl]benzoic acid ("bensulfuron"), 2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-1-methy-1H-pyrazol-4-carboxylic acid ("pyrazosulfuron"), 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]-2-thiophenecarboxylic acid ("thifensulfuron"), and 2-(2-chloroethoxy)-N[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide ("triasulfuron"); 2-(4-aryloxy-phenoxy)alkanoic acids such as (+/-)-2[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]-propanoic acid (fenoxaprop"), (+/-)-2-[4[[5-(trifluoromethyl)-2-pyridinyl]oxy]-phenoxy]propanoic acid ("fluazifop"), (+/-)-2-[4-(6chloro-2-quinoxalinyl)oxy]-phenoxy]propanoic acid ("quizalofop"), and (+ /-) -2-[(2,4-dichlorophenoxy)phenoxy]propanoic acid ("diclofop"); benzothiadiazinones such as

3-(1-methylethyl)-1H-1,2,3-benzothiadiazin-4(3H)-one-2,2-dioxide ("bentazone"); 2-chloroacetanilides such as N-(butoxymethyl)-2-chloro-N-(2,6-diethylphenyl)acetamide ("butachlor"), 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide ("metolachlor"), 2-chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide ("acetochlor"), and (*RS*)-2-chloro-N-(2,4-dimethyl-3-thienyl)-N-(2-methoxy-1-methylethyl)acetamide ("dimethenamide"); arenecarboxylic acids such as 3,6-dichloro-2-methoxybenzoic acid ("dicamba"); pyridyloxyacetic acids such as [(4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy]acetic acid ("fluroxypyr"), and other herbicides.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such as other insecticides, the other insecticides include, for example: organophosphate insecticides, such as chlorpyrifos, diazinon, dimethoate, malathion, parathion-methyl, and terbufos; pyrethroid and non-pyrethroid insecticides, such as fenvalerate, deltamethrin, fenpropathrin, cyfluthrin, flucythrinate, *alpha*-cypermethrin, bifenthrin, cypermethrin, resolved cyhalothrin, etofenprox, esfenvalerate, tralomethrin, tefluthrin, cycloprothrin, betacyfluthrin, acrinathrin and silafluofen; carbamate insecticides, such as aldicarb, carbaryl, carbofuran, and methomyl; organochlorine insecticides, such as endosulfan, endrin, heptachlor, and lindane; benzoylurea insecticides, such as diflubenuron, triflumuron, teflubenzuron, chlorfluazuron, flucycloxuron, hexaflumuron, noviflumuron, flufenoxuron, and lufenuron; and other insecticides, such as, without limitation, amitraz, clofentezine, fenpyroximate, hexythiazox, cyhexatin, spinosad, imidacloprid, chlorfenaptr, hydramethylon, acequinocyl, fenbutatin-oxide, methoxyfenozide, tebufenozide, halofenozide, indoxacarb, fipronyl, ethiprole, etoxazole, bifenazate, spirodiclofen, spiromesifen, methoprene, pyriproxyfen, fenoxycarb, pymetrozine, abamectin, emamectin benzoate, milbemectin, and other insecticides.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such as fungicides, the fungicides include, for example: benzimidazole fungicides, such as benomyl, carbendazim, thiabendazole, and thiophanate-methyl; 1,2,4-triazole fungicides, such as epoxyconazole, cyproconazole, flusilazole, flutriafol,

propiconazole, tebuconazole, triadimefon, and triadimenol; substituted anilide fungicides, such as metalaxyl, oxadixyl, procymidone, and vinclozolin; organophosphorus fungicides, such as fosetyl, iprobenfos, pyrazophos, edifenphos, and tolclofos-methyl; morpholine fungicides, such as fenpropimorph, tridemorph, and dodemorph; other systemic fungicides, such as fenarimol, imazalil, prochloraz, tricyclazole, and triforine; dithiocarbamate fungicides, such as mancozeb, maneb, propineb, zineb, and ziram; non-systemic fungicides, such as chlorothalonil, dichlofluanid, dithianon, and iprodione, captan, dinocap, dodine, fluazinam, gluazatine, PCNB, pencycuron, quintozene, tricylamide, and validamycin; inorganic fungicides, such as copper and sulphur products, and other fungicides.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such as nematicides, the nematicides include, for example: carbofuran, carbosulfan, turbufos, aldecarb, ethoprop, fenamphos, oxamyl, isazofos, cadusafos, and other nematicides.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other materials such as plant growth regulators, the plant growth regulators include, for example: maleic hydrazide, chlormequat, ethephon, gibberellin, mepiquat, thidiazon, inabenfide, triaphenthenol, paclobutrazol, unaconazol, DCPA, prohexadione, trinexapac-ethyl, and other plant growth regulators.

Soil conditioners are materials which, when added to the soil, promote a variety of benefits for the efficacious growth of plants. Soil conditioners are used to reduce soil compaction, promote and increase effectiveness of drainage, improve soil permeability, promote optimum plant nutrient content in the soil, and promote better pesticide and fertilizer incorporation. When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other materials such as soil conditioners, the soil conditioners include organic matter, such as humus, which promotes retention of cation plant nutrients in the soil; mixtures of cation nutrients, such as calcium, magnesium, potash, sodium, and hydrogen complexes; or microorganism compositions which promote conditions in the soil favorable to plant growth. Such microorganism compositions include, for

example, *bacillus, pseudomonas, azotobacter, azospirillum, rhizobium*, and soil-borne *cyanobacteria.*

Fertilizers are plant food supplements, which commonly contain nitrogen, phosphorus, and potassium. When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other materials such as fertilizers, the fertilizers include nitrogen fertilizers, such as ammonium sulfate, ammonium nitrate, and bone meal; phosphate fertilizers, such as superphosphate, triple superphosphate, ammonium sulfate, and diammonium sulfate; and potassium fertilizers, such as muriate of potash, potassium sulfate, and potassium nitrate, and other fertilizers.

In some cases, the effectiveness of such combinations may be improvement. For example, such combinations may exhibit synergistic effects, reduced rates of application resulting in improved user safety, control a broader spectrum of pests, improved tolerance by plants, and improved tolerance by non-pest species, such as mammals and fish.

The methods of the present invention are predicated on causing an insecticidal or acaricidal amount of a compound of Formula I to be present within insects or acarids and, thereby, killing or controlling the insects or acarids. It is possible and is within the scope of the invention to cause a compound of Formula I wherein R^2 represents amino (NH_2) to be present within insects or acarids by contacting the insects or acarids with a derivative of that compound, which derivative is converted within the insects or acarids to a compound of Formula I wherein N-R^3 and/or N-R^5 represents NH. Such compounds, which can be referred to as pro-insecticides, include compounds containing an R^2, R^3 and R^5 substituent that can be converted to NH_2 or NH by chemical processes, such as hydrolysis, oxidation, reduction, and the like, that are either enzymatic or non-enzymatic in nature. Suitable substituents include N-acylamino, N-substituted imino, and N-sulfenyl amino groups, and the like. Some examples, wherein hydrocarbyl refers to an aliphatic or aromatic hydrocarbon moiety optionally substituted with halogen, hydroxy, alkoxy, cyano, or nitro, or the like, are illustrated below:

NH-CO(hydrocarbyl); NH-CH(OH)(hydrocarbyl); NH-CO_2(hydrocarbyl); N=CH(hydrocarbyl); NH-CO-NH(hydrocarbyl); NH-S(hydrocarbyl); NH-$COCO_2$(hydrocarbyl); NH-S-N(hydrocarbyl)$_2$; NH-C(S-(hydrocarbyl))=N(hydrocarbyl); NH-CH(O-(hydrocarbyl))(hydrocarbyl)

Compounds containing such substituents can be prepared from compounds of Formula I wherein R^2 represents, for example, NH_2 by well established methods known to those in the art. For example, N-acyl derivatives can be prepared by treatment with an acyl halide or anhydride, N-substituted imino derivatives can be prepared by treatment with aldehydes, urea derivatives can be prepared by treatment with isocyanates, N-sulfenyl derivatives can be prepared by treatment with a sulfenyl chloride, carbamate derivatives can be prepared by treatment with a chloroformate ester, and isothiourea derivatives can be prepared by treatment with first an isothiocyanate and then a hydrocarbyl halide.

It is further possible and within the scope of the invention to cause a compound of Formula I wherein R^1 represents hydrogen (H) to be present within insects or acarids by contacting the insects or acarids with a derivative of that compound, which derivative is converted within the insects or arachnid to a compound of Formula I wherein R^1 represents hydrogen. Such compounds are also pro-insecticides. Suitable compounds include those wherein the C-H hydrogen atom of such compounds is replaced by a substituent that can be removed by hydrolysis, oxidation, or reduction in either enzymatic or non-enzymatic reactions. Typical substituents include alkoxymethyl and alkylthiomethyl groups, alkanoyloxymethyl groups, sulfenyl groups, and sulfeneamino groups. Some examples, wherein hydrocarbyl refers to an aliphatic or aromatic hydrocarbon moiety optionally substituted with halogen, hydroxy, alkoxy, cyano, or nitro, or the like are illustrated below:

CH_2-O(hydrocarbyl); S(hydrocarbyl); N-CH_2-S(hydrocarbyl); S-N(hydrocarbyl)$_2$; CH_2-OCO(hydrocarbyl); S-N(hydrocarbyl)CO_2(hydrocarbyl)

Compounds of these types can be prepared from compounds of Formula I wherein R^1 represents H by methods well established in the art. For example, alkyloxymethyl, alkylthiomethyl, and alkanoyloxymethyl substituted compounds can be prepared by alkylation with the corresponding chloromethyl alkyl ether, thioether, or ester. The sulfenyl type substituted compounds can be prepared by reaction with the corresponding sulfenyl halide.

It is further possible and within the scope of the invention to cause a compound of Formula I wherein R^2, R^3 and R^5 represents hydroxy (OH) to be present within insects or acarids by contacting the insects or acarids with a derivative of that compound, which derivative is converted within the insects or acarids to a compound of Formula I wherein R^2, R^3 and R^5 represents hydroxy. Such compounds are also pro-insecticides. Suitable compounds include compounds containing an R^2, R^3 and R^5 substituent that can be converted to OH by chemical processes, such as hydrolysis, oxidation, reduction, and the like, that are either enzymatic or non-enzymatic in nature. Typical substituents include acyloxy, carbamoyloxy, and carbonyl. Some examples, wherein hydrocarbyl refers to an aliphatic or aromatic hydrocarbon moiety optionally substituted with halogen, hydroxy, alkoxy, cyano, or nitro, or the like are illustrated below:

O-CO(hydrocarbyl; $O\text{-}CH_3$; $O\text{-}CO_2$(hydrocarbyl); $O\text{-}C(CH_3)_2$-O-hyrdocarboyl; $O\text{-}C(O)\text{-}N(\text{hydrocarbyl})_2$; $O\text{-}CH_2OCH_3$; $O\text{-}C(O)\text{-}NH_2$; $O\text{-}CH_2CH{=}CH_2$; $O\text{-}SO_3^-M^+$; $O\text{-}PO_3^-M^+$

Compounds of these types can be prepared from compounds of Formula I wherein R^2, R^3 and R^5 represents OH by methods well established in the art. For example, acyloxy derivatives may be prepared by treatment with acid halides or anhydrides; carbamoyloxy derivatives can be prepared by treatment with a carbamoyl chloride; and carbonyl derivatives can be prepared by treatment with a carbonate or chloroformate.

It is further possible and within the scope of the invention to cause a compound of Formula I wherein R^2 represents mercapto or thiol (SH) to be present within insects or acarids by contacting the insects or acarids with a derivative of that compound, which derivative is converted within the insects or acarids to a

compound of Formula I wherein R^2 represents mercapto. Such compounds are also pro-insecticides. Suitable compounds include compounds containing an R^2 substituent that can be converted to SH by chemical processes, such as hydrolysis, oxidation, reduction, and the like, that are either enzymatic or non-enzymatic in nature. Typical substituents include acylthio and hydrocarbyloxyalkylthio, wherein hydrocarbyl refers to an aliphatic or aromatic hydrocarbon moiety optionally substituted with halogen, hydroxy, alkoxy, cyano, or nitro, or the like. Some examples are illustrated below:

S-C(O)-hydrocarbyl; S-CH_2O_2C(hydrocarbyl); S-CH_3; S-C(O)-aryl

Compounds of these types can be prepared from a compound of Formula I wherein R^2 represents SH by methods well established in the art. For example, acylthio derivatives may be prepared by treatment with acyl halides or anhydrides and hydrocarbyloxyalkylthio derivatives may be prepared by treatment with a hydrocarbylheteroalkyl halide.

The present invention also includes the use of the compounds and compositions set forth herein for control of non-agricultural insect species, for example, dry wood termites and subterranean termites; as well as for use as pharmaceutical agents. In the field of veterinary medicine, the compounds of the present invention are expected to be effective against certain *endo-* and *ecto-* parasites, such as insects and worms, which prey on animals. Examples of such animal parasites include, without limitation, *Gastrophilus* spp., *Stomoxys* spp., *Trichodectes* spp., *Rhodnius* spp., Ctenocephalides canis, and other species.

The following examples further illustrate the present invention, but, of course, should not be construed as in any way limiting its scope. The examples are organized to present protocols for the synthesis of the compounds of formula I of the present invention, set forth a list of such synthesized species, and set forth certain biological data indicating the efficacy of such compounds.

EXAMPLE 1

This example illustrates one protocol for the preparation of 3-chloro-4-pyrid-3-yl-1,2,5-thiadiazole (Compound 130).

Step A 2-hydroxy-2-pyrid-3-yl-ethanenitrile

This compound was prepared in the manner described in Sauerberg et al.(Journal of Medicinal Chem., Vol. 35, No. 12, pp. 2274-2283 (1992)), namely, a stirred solution of 41.8 grams (0.64 mole) of potassium cyanide (available from Aldrich Chemical Company, Inc., Milwaukee, WI) in 175 mL of water was cooled to 5°C, and 62.5 grams (0.58 mole) of 3-pyridinecarboxaldehyde (available from Aldrich Chemical Company, Inc.) was added dropwise at a rate to maintain the reaction temperature below 5°C. Upon completion of addition, 38,5 grams (0.64 mole) of acetic acid (available from EM Sciences, Gibbstown, NJ) was added dropwise at a rated to maintain the reaction temperature below 5°C, and the reaction mixture was then stirred at 5 to 10 °C for two hours. After this time, the reaction mixture was cooled to 5°C and a yellow precipitate was collected by filtration under reduced pressure. The yellow precipitate was washed with cold water, yielding 78.27 grams (100% yield) of title compound. The NMR spectrum was consistent with the proposed structure.

Step B 2-amino-2-pyrid-3-yl-ethanenitrile

Ammonium chloride (available from J. T. Baker Inc., Phillipsburg, NJ), 113.6 grams (2.12 moles), and 52 mL (0.8 mole) of a 25% aqueous ammonium hydroxide solution (available from J. T. Baker Inc.) was taken up in 440 mL of water at ambient temperature, and then 78.2 grams (0.6 mole) of 2-hydroxy-2-pyrid-3-yl-ethanenitrile was added. Upon completion of addition, the reaction mixture was stirred at ambient temperature for about 18 hours. At the conclusion of this period, the reaction mixture was poured into a separatory funnel and extracted with several portions of methylene chloride followed by several portions of ethyl acetate. The combined extracts were dried with sodium sulfate and filtered. The filtrate was concentrated under reduced pressure, yielding 60.7 grams (78% yield) of title compound. The NMR spectrum was consistent with the proposed structure.

Step C Compound 130

Sulfur monochloride (available from Aldrich Chemical Company, Inc.), 123.1 grams (0.91 mole) was taken up in 120 mL of N,N-dimethylformamide (DMF, available from EM Sciences, Gibbstown, NJ). The mixture was cooled to 0 °C in an

ice bath, and a solution of 60.7 grams (0.5 mole) of 2-amino-2-pyrid-3-yl-ethanenitrile in 80 mL of DMF was added dropwise at a rate to maintain the reaction temperature below 10 °C. Upon completion of addition, 100 mL of methylene chloride was added. The resulting mixture was allowed to warm to ambient temperature where it stirred for about 48 hours. After this time, the reaction mixture was quenched with ice in an ice bath and then stirred for thirty minutes. At the conclusion of this period, the mixture was filtered to remove the sulfur, and the filter cake was washed thoroughly with ethyl acetate. The aqueous layer was separated from the organic layer, made basic with potassium carbonate, saturated with sodium chloride and extracted with five portions of ethyl acetate. The combined extracts were dried with magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure, yielding crude product. The crude product was purified by flash chromatography, yielding 64.1 grams (76.6% yield) of Compound 130. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 2

This example illustrates one protocol for the preparation of 3-methyl-4-pyrid-3-yl-1,2,5-thiadiazole (Compound 132).

Compound 130 (prepared in the manner of Example 1), 1.1 grams (0.006 mole), was taken up in 15 mL of tetrahydrofuran (THF, available from Aldrich Chemical Company, Inc.) at –6 °C in an ice bath containing an aqueous solution saturated with sodium chloride. Upon completion of dissolution, 2 mL (0.006 mole) of three molar methyl magnesium chloride (available from Aldrich Chemical Company, Inc.) was added during a 15 minute period. Upon completion of addition, the reaction mixture was allowed to warm to ambient temperature where it stirred for twenty minutes. At the conclusion of this period, the reaction mixture was cooled to 0 °C and 25 mL of an aqueous saturated ammonium chloride solution was slowly added. Upon completion of addition, the mixture was extracted with ethyl acetate followed by an aqueous solution saturated with sodium chloride. The combined extracts were dried with sodium sulfate and the solvent was removed under reduced pressure to yield about 1.2 grams of crude product. The crude product was purified

by column chromatography on silica gel, yielding 0.7 gram of Compound 132; mp 55-57 °C. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 3

This example illustrates one protocol for the preparation of the bromide salt of 3-chloro-4-(1-benzylpyrid-3-yl)-1,2,5-thiadiazole (Compound 162).

A solution of 1.5 grams (0.008 mole) of Compound 130 (prepared in the manner of Example 1) and 1.2 mL of (0.01 mole) of benzyl bromide (available from Aldrich Chemical Company, Inc.) in 40 mL of acetone (available from J.T. Baker Inc.) was stirred at ambient temperature for about 18 hours. After this time, most of the solvent was removed under reduced pressure to yield a residue. To the residue was added 30 mL of diethyl ether. The mixture was allowed to settle and the liquid was decanted, yielding a residue. The residue was dried under reduced pressure, yielding 1.4 grams (54% yield) of the title compound. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 4

This example illustrates one protocol for the preparation of 3-chloro-4-[1-benzyl(1,2,5,6-tetrahydropyrid-3-yl)]-1,2,5-thiadiazole (Compound 2).

Under a nitrogen atmosphere, a stirred solution of 1.4 grams (0.0039 mole) of Compound 162 (prepared in the manner of Example 3) in 30 mL of ethanol (EtOH, available from J.T. Baker Inc.) was cooled in an ice bath and 0.2 gram (0.004 mole) of sodium borohydride (available from Aldrich Chemical Company, Inc.) was added. Upon completion of addition, the reaction mixture was stirred for twenty minutes. At the conclusion of this period, the reaction mixture was allowed to warm to ambient temperature where it stirred for three hours. After this time, 40 mL of water was added and the resulting mixture was extracted with two 50 mL portions of methylene chloride. The combined extracts were dried with sodium sulfate and the solvent was removed, yielding 1.2 grams of crude product. The crude product was purified by column chromatography on silica gel, yielding 0.5 grams (38% yield) of 95% pure title compound. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 5

This example illustrates one protocol for the preparation of 3-fluoro-4-pyrid-3-yl-1,2,5-thiadiazole (Compound 131).

Compound 130 (prepared in the manner of Example 1), 0.6 gram (0.003 mole), was taken up in 3 mL of N,N-dimethylacetamide (DMAC, available from Aldrich Chemical Company). Upon completion of dissolution, 0.2 gram (0.004 mole) of potassium fluoride (available from Aldrich Chemical Company, Inc.) and 0.3 gram (0.003 mole) of tetramethylammonium chloride (available from Aldrich Chemical Company, Inc.) was added. Upon completion of addition, the reaction mixture was heated to 140 °C where it stirred 2.5 hours. At the conclusion of this period, the reaction mixture was analyzed by gas chromatography (GC), which indicated the reaction was incomplete. An additional 0.1 gram (0.0005 mole) of potassium fluoride was added and the reaction mixture was heated at 140 °C for an additional 1.5 hours. After this time, the reaction mixture was again analyzed by GC, which again indicated that the reaction was incomplete. An additional 0.06 gram (0.0003 mole) of potassium fluoride was added and the reaction mixture was heated at 140 °C for an additional hour. The reaction mixture was analyzed for a third time by GC, which indicated the reaction was incomplete. An additional 0.05 gram (0.0003 mole) of potassium fluoride was added and the reaction mixture was heated at 140 °C for an additional hour. At the conclusion of this period, the reaction mixture was diluted with 25 mL of ethyl acetate and filter through glass wool. The filtrate was combined with the filtrate from a similar experiment. The solvent was removed under reduced pressure at 40 °C. Any unreacted DMAC was removed under reduced pressure, yielding 1.86 grams of crude product. The crude product was taken up in ethyl acetate and purified by column chromatography on silica gel, yielding 0.7 gram (64% yield) of Compound 131. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 6

This example illustrates one protocol for the preparation of 3-fluoro-4-(1-methyl-1,2,5,6-tetrahydropyrid-3-yl)-1,2,5-thiadiazole (Compound 23).

Step A Iodide salt of 3-fluoro-4-(1-methylpyrid-3-yl)-1,2,5-thiadiazole

This compound was prepared in the manner of Example 3, using 0.6 gram (0.003 mole) of Compound 131 and 0.4 mL of methyl iodide (available from Aldrich Chemical Company, Inc.) in 10 mL of acetone. The yield of the title compound was 0.8 gram. The NMR spectrum was consistent with the proposed structure.

Step B Compound 23

The iodide salt of 3-fluoro-4-(1-methylpyrid-3-yl)-1,2,5-thiadiazole, 0.4 gram (0.001 mole), was taken up in 10 mL of methanol (MeOH, available from J.T. Baker Inc.) and about 8 mL of THF was added to effect dissolution. The solution was cooled to 0 °C in an ice bath and 0.07 gram (0.002 mole) of crushed sodium borohydride was added during a 12 to 15 minute period. Upon completion of addition, the reaction mixture was stirred at 0 °C for one hour. After this time, the reaction mixture was poured into 15 mL of ice and most of the organic solvents were removed under a nitrogen atmosphere. The remaining aqueous mixture was extracted with two 25 mL portions of ethyl acetate. The combined extracts were dried with sodium sulfate and concentrated under reduced pressure to yield the crude product. The crude product was purified by column chromatography on silica gel, yielding 0.09 to 0.1 gram of Compound 23. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 7

This example illustrates one protocol for the preparation of 3-pyrid-3-yl-1,2,5-thiadiazole (Compound 129).

To a stirred solution of 0.3 gram (0.002 mole) of Compound 130 (prepared in the manner of Example 1) in 6 mL of MeOH was added 0.3 gram (0.005 mole) of sodium thiomethoxide (available from Fluka Chemical Corp., Ronkonkoma, NY). Upon completion of addition, the reaction mixture was stirred at ambient temperature for about 18 hours. After this time, the reaction mixture was refluxed for two hours. Upon completion of this period, the reaction mixture was analyzed by thin layer chromatography (TLC), which indicated that the reaction was complete. The reaction mixture was poured into water and extracted with three portions ethyl acetate. The combined extracts were dried with magnesium sulfate and filtered. The

filtrate was concentrated under reduced pressure, yielding 0.17 gram (68% yield) of Compound 129. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 8

This example illustrates one protocol for the preparation of 3-[1-methyl(1,2,5,6-tetrahydropyrid-3-yl)]-1,2,5-thiadiazole (Compound 4).

Step A Iodide salt of 4-(1-methylpyrid-3-yl)-1,2,5-thiadiazole

This compound was prepared in the manner of Example 3, using 0.14 gram (0.0009 mole) of Compound 129 and 0.3 mL of methyl iodide in 5 mL of acetone. The yield of the title compound was 0.2 gram. The NMR spectrum was consistent with the proposed structure.

Step B Compound 4

This compound was prepared in the manner of Example 4, using 0.2 gram (0.0005 mole) of the iodide salt of 4-(1-methylpyrid-3-yl)-1,2,5-thiadiazole and 0.06 gram (0.002 mole) of sodium borohydride in 20 mL of ethanol. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 9

This example illustrates one protocol for the preparation of 3-chloro-4-(3-chloroquinuclidin-3-yl)-1,2,5-thiadiazole (Compound 103).

Step A Hydrochloride salt of ethyl 2-cyano-2-quinuclidin-3-ylideneacetate

This compound was prepared in the manner described in Olesen et al. (Eur. J. Med. Chem., 31, pp. 221-230 (1996)), namely, to a stirred solution of 26.9 grams (0.2 mole) of 3-quinuclidinone hydrochloride (available from Aldrich Chemical Company, Inc.) and 35.4 mL (0.03 mole) of ethyl cyanoacetate (available from Aldrich Chemical Company) was added 46.4 mL of triethylamine (TEA, available from J.T. Baker Inc.). Upon completion of addition, the reaction mixture was heated to 80 °C where it stirred for two hours. At the conclusion of this period, the reaction mixture was diluted with water and extracted with three portions of ethyl acetate. The extracts were combined, dried with magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure, yielding 39.8 grams of reddish viscous oil. The reddish viscous oil was diluted with diethyl ether and a 1.0 M solution of

hydrogen chloride in diethyl ether was added. The resulting mixture was cooled to ambient temperature where it was allowed to stand for about 18 hours. After this time, the mixture was scratched with a spatula several times to yield a pinkish granular solid. The solid was filtered and dried under reduced pressure, yielding 41.91 grams (98.1% yield) of title compound; mp 192-194 °C. The NMR spectrum was consistent with the proposed structure.

Step B Hydrochloride salt of ethyl 2-cyano-2-quinuclidin-3-ylacetate

Under a nitrogen atmosphere, to 0.4 gram of 10% palladium on carbon was added a solution of 41.9 grams (0.02 mole) of the hydrochloride salt of ethyl 2-cyano-2-quinuclidin-3-ylideneacetate bottle in 225 mL of EtOH. Upon completion of addition, the reaction mixture was hydrogenated in a Parr hydrogenator. When it was noticed that the hydrogenation was proceeding slowly, an additional 0.3 gram of 5% palladium on carbon was added to the reaction mixture to drive the hydrogenation to completion. Upon completion of the hydrogenation, the reaction mixture was filtered, and the filtrate was concentrated under reduced pressure, yielding 42 grams (99% yield) of title compound. The NMR spectrum was consistent with the proposed structure.

Step C Compound 103

This compound was prepared in the manner described in Olesen et al. (Eur. J. Med. Chem., 31, pp. 221-230 (1996)), namely, under a nitrogen atmosphere, 8.7 grams (0.4 mole) of sodium (available from Aldrich Chemical Company, Inc.) was added in portions to 200 mL of a 1:1 mixture of MeOH and EtOH. To the resulting mixture was added 42.0 grams (0.2 mole) of the hydrochloride salt of ethyl 2-cyano-2-quinuclidin-3-ylacetate. Upon completion of addition, the resulting solution was stirred for thirty minutes. After this time, the mixture was cooled to 0-5 °C in an ice bath and 33 mL of isoamyl nitrite (available from Aldrich Chemical Company, Inc.) was added dropwise at a rate to maintain the reaction temperature below 10 °C. Upon completion of addition, the reaction mixture was concentrated under reduced pressure and toluene was added. The resulting mixture was again concentrated under reduced pressure, yielding a residue. The residue was taken up in DMF. The

resulting solution was added dropwise to a solution of 76.6 grams (0.6 mole) of sulfur monochloride in 80 mL of DMF at rate to maintain the reaction temperature at or below 0 °C. Upon completion of addition, the reaction mixture was allowed to warm to ambient temperature where it stirred for about 48 hours. At the conclusion of this period, 100 mL of water was carefully added. The reaction mixture was warmed to 70 °C and filtered. The filtrate was diluted with water and made basic with potassium carbonate. The basic mixture was extracted with three portions of ethyl acetate. The combined extracts were dried with magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure, yielding a dark reddish black viscous oil. The residue was purified by flash chromatography, yielding 10.0 grams of Compound 103; mp 93-95 °C. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 10

This example illustrates one protocol for the preparation of 3-chloro-4-quinuclidin-3-yl-1,2,5-thiadiazole (Compound 102).

Under a nitrogen atmosphere, a mixture of 0.3 gram of 10% palladium on carbon, 0.2 gram of 5% palladium on carbon, 7.4 grams (0.03 mole) of Compound 103, 80 mL of ethyl acetate, 30 mL of TEA, and 30 mL of methylene chloride (available from J.T. Baker Inc.) was hydrogenated in a Parr hydrogenator. When it was noticed that the hydrogenation had stalled, an additional 4.0 grams of 10% palladium on carbon, 0.3 gram of 5% palladium on carbon and 1.0 gram (0.004 mole) of Compound 106 were added. Upon completion of addition, the reaction mixture was hydrogenated for about 48 hours. After this time, the reaction mixture was analyzed by GC and TLC, which indicated that the hydrogenation was complete. The reaction mixture was filtered. The filtrate was concentrated under reduced pressure to yield a residue. The residue was taken up in water, made basic with potassium carbonate, and extracted with three portions of methylene chloride. The extracts were combined, dried with magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure, yielding 6.0 grams (92.9% yield) of Compound 102. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 11

This example illustrates one protocol for the preparation of 3-butoxy-4-quinuclidin-3-yl-1,2,5-thiadiazole (Compound 110).

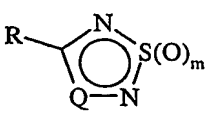
Normal (n)-Butanol (available from J.T. Baker Inc.), 5 mL, was chilled in an ice bath, and 0.1 gram (0.025 mole) of 60% sodium hydride in oil (available from Aldrich Chemical Company, Inc.) followed by 0.3 gram (0.001 mole) of Compound 102 was added. Upon completion of addition, the reaction mixture was allowed to warm to ambient temperature where it stirred for about 48 hours. At the conclusion of this period, the reaction mixture was heated to 60 °C where it stirred for four hours. After this time, the reaction mixture was analyzed by GC, which indicated that none of the starting material was present. The solvent was removed under reduced pressure, yielding a residue. The residue was taken up in ethyl acetate and washed with an aqueous concentrated sodium chloride solution. The organic layer was separated and the solvent was removed under reduced pressure, yielding an orange oil. The orange oil was purified by column chromatography on silica gel, yielding Compound 110. The NMR spectrum was consistent with the proposed structure.

It is well known to one of ordinary skill in the art that the compounds of formula I of the present invention can contain optically-active and racemic forms. It is also well known in the art that the compounds of formula I may contain stereoisomeric forms and/or exhibit polymorphism. It is to be understood that the present invention encompasses any racemic, optically-active, polymorphic or stereoisomeric form, or mixtures thereof. It should be noted that it is well known in the art how to prepare optically-active forms, for example by resolution of a racemic mixture or by synthesis from optically-active starting materials.

The following table sets forth some compounds of formula I:

Table 1

Pesticidal 1,2,5-Thiadiazole Derivatives



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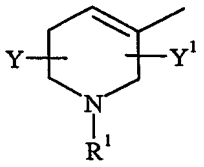
where R is a azabicyclic selected from the following structures:



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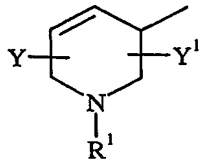

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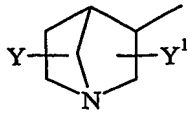

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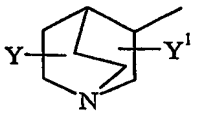

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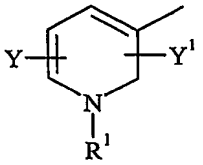

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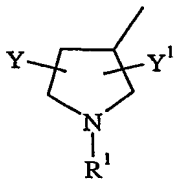

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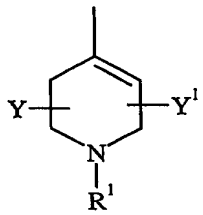

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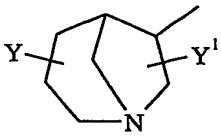

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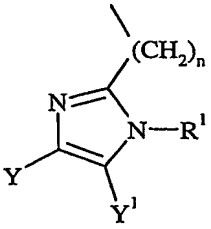

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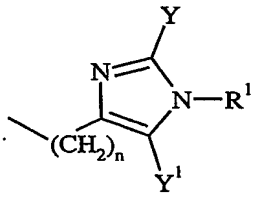

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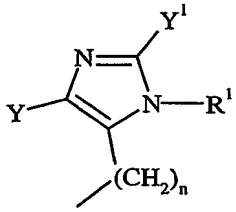

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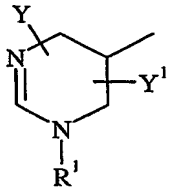

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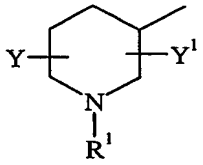

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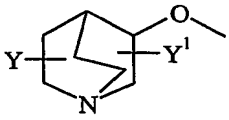

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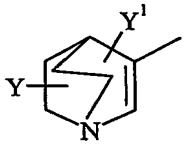

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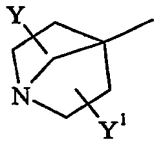

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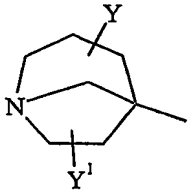
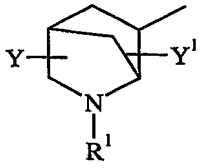
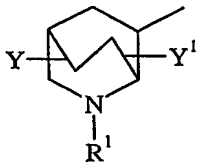


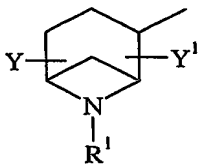
W17



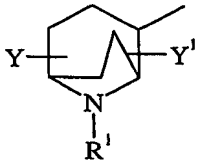
W18



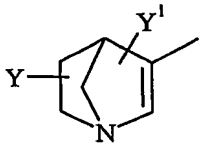
W19



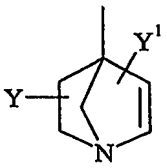
W20



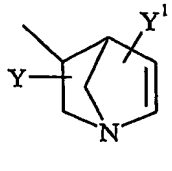
W21



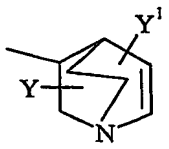
W22



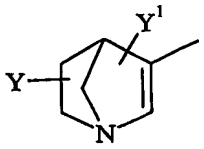
W23



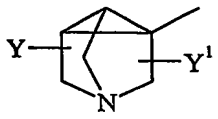
W24



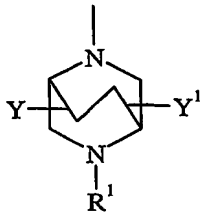
W25



W26

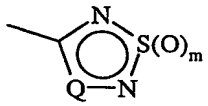


W27

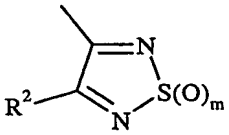


W28

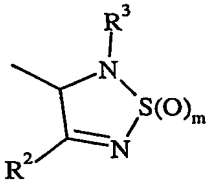
and where



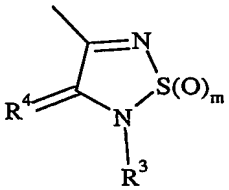
is a 1,2,5-thiadiazole where Q is CR^2 or $C=R^4$, where the 1,2,5-thiadiazole is selected from



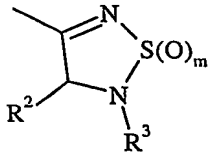
Ia
a 1,2,5-thiadiazol-3-yl



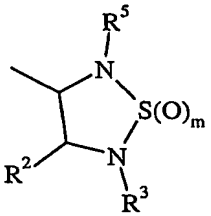
Ib
a 1,2,5-thiadiazolin-3-yl



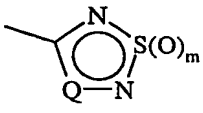
Ic
a 1,2,5-thiadiazolin-3-R^4-4-yl

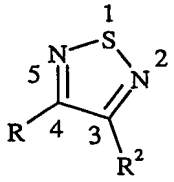


Id
a 1,2,5-thiadiazolin-4-yl



Ie
a 1,2,5-thiadiazolidin-3-yl

where  is Ia;



I

where m is 0:

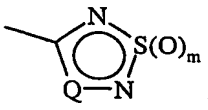
Cmpd. No.	R	R^1	R^2	Y	Y^1
1	W1	H	Cl	H	H
2	W1	$-CH_2C_6H_5$	Cl	H	H
3	W1	$-C(O)OC_2H_5$	Cl	H	H
4	W1	$-CH_3$	H	H	H
5	W1	$-CH_3$	H	2-Cl	H
6	W1	$-CH_3$	H	2-F	H
7	W1	$-CH_3$	H	$2-CH_3$	H
8	W1	$-CH_3$	H	4-Cl	H
9	W1	$-CH_3$	H	4-F	H
10	W1	$-CH_3$	H	$4-CH_3$	H
11	W1	$-CH_3$	H	6-Cl	H
12	W1	$-CH_3$	H	6-F	H
13	W1	$-CH_3$	H	$6-CH_3$	H
14	W1	$-CH_3$	H	2-Cl	2-Cl
15	W1	$-CH_3$	H	2-F	2-F
16	W1	$-CH_3$	H	$2-CH_3$	$2-CH_3$
17	W1	$-CH_3$	H	6-Cl	6-Cl
18	W1	$-CH_3$	H	6-F	6-F
19	W1	$-CH_3$	H	$6-CH_3$	$6-CH_3$
20	W1	$-C_2H_5$	H	H	H
21	W1	$-CH_2OCH_3$	H	H	H
22	W1	$-CH_3$	Cl	H	H
23	W1	$-CH_3$	F	H	H
24	W1	$-CH_3$	F	2-Cl	H
25	W1	$-CH_3$	F	2-F	H
26	W1	$-CH_3$	F	$2-CH_3$	H
27	W1	$-CH_3$	F	4-Cl	H
28	W1	$-CH_3$	F	4-F	H
29	W1	$-CH_3$	F	$4-CH_3$	H
30	W1	$-CH_3$	F	6-Cl	H
31	W1	$-CH_3$	F	6-F	H
32	W1	$-CH_3$	F	$6-CH_3$	H
33	W1	$-CH_3$	F	2-Cl	2-Cl
34	W1	$-CH_3$	F	2-F	2-F
35	W1	$-CH_3$	F	$2-CH_3$	$2-CH_3$
36	W1	$-CH_3$	F	6-Cl	6-Cl
37	W1	$-CH_3$	F	6-F	6-F
38	W1	$-CH_3$	F	$6-CH_3$	$6-CH_3$
39	W1	$-CH_3$	$-CH_3$	H	H
40	W1	$-CH_3$	$-CH_3$	2-Cl	H
41	W1	$-CH_3$	$-CH_3$	2-F	H
42	W1	$-CH_3$	$-CH_3$	$2-CH_3$	H
43	W1	$-CH_3$	$-CH_3$	4-Cl	H
44	W1	$-CH_3$	$-CH_3$	4-F	H
45	W1	$-CH_3$	$-CH_3$	$4-CH_3$	H
46	W1	$-CH_3$	$-CH_3$	6-Cl	H
47	W1	$-CH_3$	$-CH_3$	6-F	H
48	W1	$-CH_3$	$-CH_3$	$6-CH_3$	H
49	W1	$-CH_3$	$-CH_3$	2-Cl	2-Cl
50	W1	$-CH_3$	$-CH_3$	2-F	2-F
51	W1	$-CH_3$	$-CH_3$	$2-CH_3$	$2-CH_3$

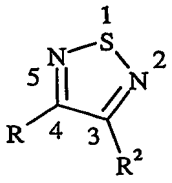
Cmpd. No.	R	R^1	R^2	Y	Y^1
52	W1	$-CH_3$	$-CH_3$	6-Cl	6-Cl
53	W1	$-CH_3$	$-CH_3$	6-F	6-F
54	W1	$-CH_3$	$-CH_3$	$6-CH_3$	$6-CH_3$
55	W1	$-CH_3$	$-CH_2CH_2C_6H_5$	H	H
56	W1	$-CH_3$	$-OCH_3$	H	H
57[1]	W1	$-CH_3$	$-OCH_3$	H	H
58	W1	$-CH_3$	$-OC_2H_5$	H	H
59	W1	$-CH_3$	$-OC_3H_7$	H	H
60	W1	$-CH_3$	$-OC_4H_9$	H	H
61	W1	$-CH_3$	$-OC_5H_{11}$	H	H
62	W1	$-CH_3$	$-OC_6H_{13}$	H	H
63	W1	$-CH_3$	4-FPhO-	H	H
64	W1	$-CH_3$	$-OCH_2CH=CH_2$	H	H
65[1]	W1	$-CH_3$	$-OCH_2CH=CH_2$	H	H
66	W1	$-CH_3$	$-OCH_2C\equiv CH$	H	H
67	W1	$-CH_3$	$-OCH_2C\equiv CCH_3$	H	H
68	W1	$-CH_3$	$-OCH_2CH_2C\equiv CH$	H	H
69	W1	$-CH_3$	$-SCH_3$	H	H
70	W1	$-CH_3$	$-SC_2H_5$	H	H
71	W1	$-CH_3$	$-SC_3H_7$	H	H
72	W1	$-CH_3$	$-SC_4H_9$	H	H
73	W1	$-CH_3$	$-SC_5H_{11}$	H	H
74	W1	$-CH_3$	$-SC_5H_{10}CN$	H	H
75	W1	$-CH_3$	$-SC_6H_{13}$	H	H
76	W1	$-CH_3$	$-SC_6H_{12}CN$	H	H
77	W1	$-CH_3$	$-SCH_2CH=CH_2$	H	H
78	W1	$-CH_3$	$-SCH_2C\equiv CH$	H	H
79	W2	$-CH_3$	$-C(O)OC_4H_9$	H	H
80	W3	---	H	H	H
81	W3	---	H	2-Cl	H
82	W3	---	H	2-F	H
83	W3	---	H	$2-CH_3$	H
84	W3	---	H	4-Cl	H
85	W3	---	H	4-F	H
86	W3	---	H	$4-CH_3$	H
87	W3	---	H	6-Cl	H
88	W3	---	H	6-F	H
89	W3	---	H	$6-CH_3$	H
90	W3	---	H	2-Cl	2-Cl
91	W3	---	H	2-F	2-F
92	W3	---	H	$2-CH_3$	$2-CH_3$
93	W3	---	H	6-Cl	6-Cl
94	W3	---	H	6-F	6-F
95	W3	---	H	$6-CH_3$	$6-CH_3$
96	W3	---	Cl	H	H
97	W3	---	F	H	H
98	W3	---	CH3	H	H
99	W3	---	$-OCH_2C\equiv CH$	H	H
100	W4	---	H	H	H
101	W4	---	F	H	H
102	W4	---	Cl	H	H
103	W4	---	Cl	3-Cl	H
104[2]	W4	---	Cl	3-Cl	H
105	W4	---	Cl	2-Cl	2-Cl
106	W4	---	Cl	$6-CH_3$	$6-CH_3$

Cmpd. No.	R	R^1	R^2	Y	Y^1
107	W4	---	$-OCH_3$	H	H
108	W4	---	$-OC_2H_5$	H	H
109	W4	---	$-OC_3H_7$	H	H
110	W4	---	$-OC_4H_9$	H	H
111	W4	---	$-OC_5H_{11}$	H	H
112	W4	---	$-OC_6H_{13}$	H	H
113	W4	---	$-OCH_2CH=CH_2$	H	H
114	W4	---	$-OCH_2C\equiv CH$	H	H
115	W4	---	$-OCH_2C\equiv CCH_3$	H	H
116	W4	---	$-OCH_2CH_2C\equiv CH$	H	H
117	W4	---	$-SCH_3$	H	H
118	W4	---	$-SC_2H_5$	H	H
119	W4	---	$-SC_3H_7$	H	H
120	W4	---	$-SC_4H_9$	H	H
121	W4	---	$-SC_5H_{11}$	H	H
122	W4	---	$-SC_5H_{10}CN$	H	H
123	W4	---	$-SC_6H_{13}$	H	H
124	W4	---	$-SC_6H_{12}CN$	H	H
125	W4	---	$-SCH_2CH=CH_2$	H	H
126	W4	---	$-SCH_2C\equiv CH$	H	H
127	W4	---	$-SCH_2C\equiv CCH_3$	H	H
128	W4	---	$-SCH_2CH_2C\equiv CH$	H	H
129	W5	H	H	H	H
130	W5	H	Cl	H	H
131	W5	H	F	H	H
132	W5	H	$-CH_3$	H	H
133	W5	H	$-C_2H_5$	H	H
134	W5	H	$-C_3H_7$	H	H
135	W5	H	$-C_4H_9$	H	H
136	W5	H	$-C_5H_{11}$	H	H
137	W5	H	$-SC_6H_{13}$	H	H
138	W5	H	$-OCH_3$	H	H
139	W5	H	$-OC_2H_5$	H	H
140	W5	H	$-OC_3H_7$	H	H
141[3]	W5	$-CH_3$	$-OC_3H_7$	H	H
142	W5	H	$-OC_4H_9$	H	H
143	W5	H	$-OC_5H_{11}$	H	H
144	W5	H	$-OC_6H_{13}$	H	H
145	W5	H	$-OCH_2CH=CH_2$	H	H
146[3]	W5	$-CH_3$	$-OCH_2CH=CH_2$	H	H
147	W5	H	$-OCH_2C\equiv CCH_3$	H	H
148	W5	H	$-OCH_2CH_2C\equiv CH$	H	H
149	W5	H	$-SCH_3$	H	H
150	W5	H	$-SC_2H_5$	H	H
151	W5	H	$-SC_3H_7$	H	H
152	W5	H	$-SC_4H_9$	H	H
153	W5	H	$-SC_5H_{11}$	H	H
154	W5	H	$-SC_5H_{10}CN$	H	H
155	W5	H	$-SC_6H_{13}$	H	H
156	W5	H	$-SC_6H_{12}CN$	H	H
157	W5	H	$-SCH_2CH=CH_2$	H	H
158	W5	H	$-SCH_2C\equiv CH$	H	H
159	W5	H	$-SCH_2C\equiv CCH_3$	H	H
160	W5	H	$-SCH_2CH_2C\equiv CH$	H	H
161[4]	W5	$-C(O)OC_2H_5$	Cl	H	H

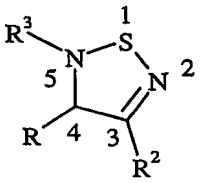
Cmpd. No.	R	R^1	R^2	Y	Y^1
162[5]	W5	$-CH_2C_6H_5$	Cl	H	H
163	W6	H	H	H	H
164	W6	H	Cl	H	H
165	W6	H	F	H	H
166	W6	H	$-CH_3$	H	H
167	W6	H	$-OCH_2C\equiv CCH_3$	H	H
168	W6	$-CH_3$	H	H	H
169	W6	$-CH_3$	Cl	H	H
170	W6	$-CH_3$	F	H	H
171	W6	$-CH_3$	$-CH_3$	H	H
172	W6	$-CH_3$	$-OCH_2C\equiv CCH_3$	H	H
173	W7	H	H	H	H
174	W7	H	Cl	H	H
175	W7	H	Cl	4-Cl	H
1776	W7	H	F	H	H
177	W7	H	$-CH_3$	H	H
178	W7	H	$-OCH_2C\equiv CH$	H	H
179	W7	$-CH_3$	H	H	H
180	W7	$-CH_3$	Cl	H	H
181	W7	$-CH_3$	Cl	H	H
182	W7	$-CH_3$	F	H	H
183	W7	$-CH_3$	$-CH_3$	H	H
184	W7	$-CH_3$	$-OCH_2C\equiv CH$	H	H
185	W7	$-CH_3$	$-CH_3$	2-Cl	H
186	W7	$-CH_3$	$-CH_3$	2-F	H
187	W7	$-CH_3$	$-CH_3$	$2-CH_3$	H
188	W7	$-CH_3$	$-CH_3$	4-Cl	H
189	W7	$-CH_3$	$-CH_3$	4-F	H
190	W7	$-CH_3$	$-CH_3$	$4-CH_3$	H
191	W7	$-CH_3$	$-CH_3$	6-Cl	H
192	W7	$-CH_3$	$-CH_3$	6-F	H
193	W7	$-CH_3$	$-CH_3$	$6-CH_3$	H
194	W7	$-CH_3$	$-CH_3$	2-Cl	2-Cl
195	W7	$-CH_3$	$-CH_3$	2-F	2-F
196	W7	$-CH_3$	$-CH_3$	$2-CH_3$	$2-CH_3$
197	W7	$-CH_3$	$-CH_3$	6-Cl	6-Cl
198	W7	$-CH_3$	$-CH_3$	6-F	6-F
199	W7	$-CH_3$	$-CH_3$	$6-CH_3$	$6-CH_3$
200	W8	---	H	H	H
201	W8	---	Cl	H	H
202	W8	---	F	H	H
203	W8	---	$-CH_3$	H	H
204	W8	---	$-OCH_2C\equiv CH$	H	H

[1]carboxylic acid salt; [2]HCl salt; [3]iodide salt; [4]boron tetrafluoride salt; [5]bromide salt

where  is Ia or Ib



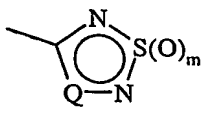
Derived from Ia, where m is 0

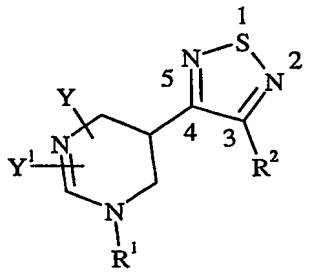


Derived from Ib, where m is 0

Cmpd. No	Formula	R	R^2	R^3	R^1	n
205	Ia	W9	H	---	H	0
206	Ia	W9	Cl	---	H	0
207	Ia	W9	F	---	H	0
208	Ia	W9	$-CH_3$	---	H	0
209	Ia	W9	$-C_2H_5$	---	H	0
210	Ia	W9	$-OCH_3$	---	H	0
211	Ia	W9	$-CH_2OCH$	---	H	0
212	Ia	W9	$-OCH_2C\equiv CH$	---	H	0
213	Ia	W9	H	---	H	1
214	Ia	W9	Cl	---	H	1
215	Ia	W9	F	---	H	1
216	Ia	W9	$-CH_3$	---	H	1
217	Ia	W9	$-C_2H_5$	---	H	1
218	Ia	W9	$-OCH_3$	---	H	1
219	Ia	W9	$-CH_2OCH$	---	H	1
220	Ia	W9	$-OCH_2C\equiv CH$	---	H	1
221	Ia	W9	H	---	$-CH_3$	0
222	Ia	W9	Cl	---	$-CH_3$	0
223	Ia	W9	F	---	$-CH_3$	0
224	Ia	W9	$-CH_3$	---	$-CH_3$	0
225	Ia	W9	$-C_2H_5$	---	$-CH_3$	0
226	Ia	W9	$-OCH_3$	---	$-CH_3$	0
227	Ia	W9	$-CH_2OCH$	---	$-CH_3$	0
228	Ia	W9	$-OCH_2C\equiv CH$	---	$-CH_3$	0
229	Ib	W9	H	$-CH_2CH_2O-$		0
230	Ib	W9	H	H	$-CH_3$	1
231	Ia	W9	Cl	---	$-CH_3$	1
232	Ia	W9	F	---	$-CH_3$	1
233	Ia	W9	$-CH_3$	---	$-CH_3$	1
234	Ia	W9	$-C_2H_5$	---	$-CH_3$	1
235	Ia	W9	$-OCH_3$	---	$-CH_3$	1
236	Ia	W9	$-CH_2OCH$	---	$-CH_3$	1
237	Ia	W9	$-OCH_2C\equiv CH$	---	$-CH_3$	1
238	Ia	W9	H	---	$-CH_3$	2
239	Ia	W9	Cl	---	$-CH_3$	2
240	Ia	W9	F	---	$-CH_3$	2
241	Ia	W9	$-CH_3$	---	$-CH_3$	2
242	Ia	W9	$-C_2H_5$	---	$-CH_3$	2
243	Ia	W9	$-OCH_3$	---	$-CH_3$	2
244	Ia	W9	$-CH_2OCH$	---	$-CH_3$	2
245	Ia	W9	$-OCH_2C\equiv CH$	---	$-CH_3$	2
246	Ia	W10	H	---	$-CH_3$	0
247	Ia	W10	Cl	---	$-CH_3$	0
248	Ia	W10	F	---	$-CH_3$	0
249	Ia	W10	$-CH_3$	---	$-CH_3$	0

Cmpd. No	Formula	R	R^2	R^3	R^1	n
250	Ia	W10	$-C_2H_5$	---	$-CH_3$	0
251	Ia	W10	$-OCH_3$	---	$-CH_3$	0
252	Ia	W10	$-CH_2OCH$	---	$-CH_3$	0
253	Ia	W10	$-OCH_2C\equiv CH$	---	$-CH_3$	0
254	Ib	W10	H	$-CH_2CH_2O-$		0
255	Ib	W10	H	$-CH_3$	$-CH_3$	1
256	Ia	W10	Cl	---	$-CH_3$	1
257	Ia	W10	F	---	$-CH_3$	1
258	Ia	W10	$-CH_3$	---	$-CH_3$	1
259	Ia	W10	$-C_2H_5$	---	$-CH_3$	1
260	Ia	W10	$-OCH_3$	---	$-CH_3$	1
261	Ia	W10	$-CH_2OCH$	---	$-CH_3$	1
262	Ia	W10	$-OCH_2C\equiv CH$	---	$-CH_3$	1
263	Ia	W10	H	---	$-CH_3$	2
264	Ia	W10	Cl	---	$-CH_3$	2
265	Ia	W10	F	---	$-CH_3$	2
266	Ia	W10	$-CH_3$	---	$-CH_3$	2
267	Ia	W10	$-C_2H_5$	---	$-CH_3$	2
268	Ia	W10	$-OCH_3$	---	$-CH_3$	2
269	Ia	W10	$-CH_2OCH$	---	$-CH_3$	2
270	Ia	W10	$-OCH_2C\equiv CH$	---	$-CH_3$	2
271	Ia	W11	H	---	$-CH_3$	0
272	Ia	W11	Cl	---	$-CH_3$	0
273	Ia	W11	F	---	$-CH_3$	0
274	Ia	W11	$-CH_3$	---	$-CH_3$	0
275	Ia	W11	$-C_2H_5$	---	$-CH_3$	0
276	Ia	W11	$-OCH_3$	---	$-CH_3$	0
277	Ia	W11	$-CH_2OCH$	---	$-CH_3$	0
278	Ia	W11	$-OCH_2C\equiv CH$	---	$-CH_3$	0
279	Ib	W11	H	$-CH_2CH_2O-$		0
280	Ib	W11	H	$-NH_2$	$-CH_3$	1
281	Ia	W11	Cl	---	$-CH_3$	1
282	Ia	W11	F	---	$-CH_3$	1
283	Ia	W11	$-CH_3$	---	$-CH_3$	1
284	Ia	W11	$-C_2H_5$	---	$-CH_3$	1
285	Ia	W11	$-OCH_3$	---	$-CH_3$	1
286	Ia	W11	$-CH_2OCH$	---	$-CH_3$	1
287	Ia	W11	$-OCH_2C\equiv CH$	---	$-CH_3$	1
288	Ia	W11	H	---	$-CH_3$	2
289	Ia	W11	Cl	---	$-CH_3$	2
290	Ia	W11	F	---	$-CH_3$	2
291	Ia	W11	$-CH_3$	---	$-CH_3$	2
292	Ia	W11	$-C_2H_5$	---	$-CH_3$	2
293	Ia	W11	$-OCH_3$	---	$-CH_3$	2
294	Ia	W11	$-CH_2OCH$	---	$-CH_3$	2
295	Ia	W11	$-OCH_2C\equiv CH$	---	$-CH_3$	2

where R is W12 and  is Ia ;

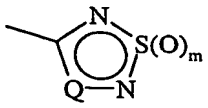


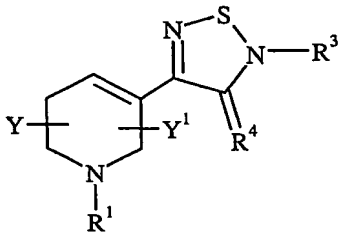
I

where Y and Y^1 are hydrogen, and m is 0:

Cmpd. No.	R^1	R^2
296	H	H
297	H	$-CH_3$
298	H	$-C_2H_5$
299	H	$-OCH_3$
300	H	$-CH_2OCH$
301	H	$-OCH_2C\equiv CH$
302	H	$-C(O)OC_4H_9$
303	Cl	H
304	Cl	$-CH_3$
305	Cl	$-C_2H_5$
306	Cl	$-OCH_3$
307	Cl	$-CH_2OCH$
308	Cl	$-OCH_2C\equiv CH$
309	Cl	$-C(O)OC_4H_9$
310	F	H
311	F	$-CH_3$
312	F	$-C_2H_5$
313	F	$-OCH_3$
314	F	$-CH_2OCH$
315	F	$-OCH_2C\equiv CH$
316	F	$-C(O)OC_4H_9$
317	$-CH_3$	H
318	$-CH_3$	$-CH_3$
319	$-CH_3$	$-C_2H_5$
320	$-CH_3$	$-OCH_3$
321	$-CH_3$	$-CH_2OCH$
322	$-CH_3$	$-OCH_2C\equiv CH$
323	$-CH_3$	$-C(O)OC_4H_9$
324	$-OCH_3$	H
325	$-OCH_3$	$-CH_3$
326	$-OCH_3$	$-C_2H_5$
327	$-OCH_3$	$-OCH_3$
328	$-OCH_3$	$-CH_2OCH$
329	$-OCH_3$	$-OCH_2C\equiv CH$
330	$-OCH_3$	$-C(O)OC_4H_9$
331	$-CH_2OCH$	H
332	$-CH_2OCH$	$-CH_3$
333	$-CH_2OCH$	$-C_2H_5$
334	$-CH_2OCH$	$-OCH_3$
335	$-CH_2OCH$	$-CH_2OCH$
336	$-CH_2OCH$	$-OCH_2C\equiv CH$
337	$-CH_2OCH$	$-C(O)OC_4H_9$

Cmpd. No.	R^1	R^2
338	$-OCH_2C\equiv CH$	H
339	$-OCH_2C\equiv CH$	$-CH_3$
340	$-OCH_2C\equiv CH$	$-C_2H_5$
341	$-OCH_2C\equiv CH$	$-OCH_3$
342	$-OCH_2C\equiv CH$	$-CH_2OCH$
343	$-OCH_2C\equiv CH$	$-OCH_2C\equiv CH$
344	$-OCH_2C\equiv CH$	$-C(O)OC_4H_9$

where R is W1 and  is Ic :



I

where Y and Y^1 are hydrogen, and m is 0:

Cmpd. No.	R^1	R^3	R^4	R^{10}
345	H	H	O	---
346	$-CH_3$	H	O	---
347	$-CH_3$	$-CH_3$	O	---
348	$-CH_3$	$-C_6H_5$	O	---
349	$-CH_3$	$-NH_2$	O	---
350	$-CH_3$	$-N(CH_3)_2$	O	---
351	$-CH_3$	$-N(C_2H_5)_2$	O	---
352	$-CH_3$	$-N(CH_3)_2$	O	---
353	$-CH_3$	-OH	O	---
354	$-CH_3$	$-OCH_3$	O	---
355	$-CH_3$	$-OCH_2C\equiv CH$	O	---
356	$-C_2H_5$	$-C_2H_5$	O	---
357	H	H	S	---
358	$-CH_3$	H	S	---
359	$-CH_3$	$-CH_3$	S	---
360	$-CH_3$	$-C_6H_5$	S	---
361	$-CH_3$	$-NH_2$	S	---
362	$-CH_3$	$-N(CH_3)_2$	S	---
363	$-CH_3$	$-N(C_2H_5)_2$	S	---
364	$-CH_3$	$-N(CH_3)_2$	S	---
365	$-CH_3$	-OH	S	---
366	$-CH_3$	$-OCH_3$	S	---

Cmpd. No.	R^1	R^3	R^4	R^{10}
367	$-CH_3$	$-OCH_2C\equiv CH$	S	---
368	$-C_2H_5$	$-C_2H_5$	S	---
369	H	H	$-NR^{10}$	H
370	$-CH_3$	H	$-NR^{10}$	CH_3
371	$-CH_3$	$-CH_3$	$-NR^{10}$	CH_3
372	$-CH_3$	$-C_6H_5$	$-NR^{10}$	CH_3
373	$-CH_3$	$-NH_2$	$-NR^{10}$	CH_3
374	$-CH_3$	$-N(CH_3)_2$	$-NR^{10}$	CH_3
375	$-CH_3$	$-N(C_2H_5)_2$	$-NR^{10}$	CH_3
376	$-CH_3$	$-N(CH_3)_2$	$-NR^{10}$	CH_3
377	$-CH_3$	-OH	$-NR^{10}$	CH_3
378	$-CH_3$	$-OCH_3$	$-NR^{10}$	CH_3
379	$-CH_3$	$-OCH_2C\equiv CH$	$-NR^{10}$	CH_3
380	$-C_2H_5$	$-C_2H_5$	$-NR^{10}$	C_2H_5
381	$-CH_3$	$-CH_3$	$-NR^{10}$	$CH_2CH_2C_6H_5$
382	$-CH_3$	$-C_6H_5$	$-NR^{10}$	OCH_3
383	$-CH_3$	$-OCH_2C\equiv CH$	$-NR^{10}$	$OCH_2CH=CH_2$
384	$-CH_3$	$-CH_3$	$-NR^{10}$	$NOCH_2C\equiv CH$
385	$-CH_3$	$-NH_2$	$-NR^{10}$	$OCH_2C\equiv CCH_3$
386	$-CH_3$	$-N(CH_3)_2$	$-NR^{10}$	$OCH_2CH_2C\equiv CH$

The following table sets forth physical characterizing data for certain compounds of formula I of the present invention. The compounds of formula I are identified by numbers that correspond to those in Table 1:

Characterizing Data

Compound No.	Empirical Formula	Melting Point/Physical State
1	$C_7H_8ClN_3S$	OIL
2	$C_{14}H_{14}ClN_3S$	SOLID
3	$C_{10}H_{12}ClN_3O_2S$	71-72 °C
4	$C_8H_{11}N_3S$	OIL
22	$C_8H_{10}ClN_3S$	LIQUID
23	$C_8H_{10}FN_3S$	LIGHT BROWN OIL
39	$C_9H_{13}N_3S$	LIGHT BROWN OIL
55	$C_{16}H_{19}N_3S$	BROWN OIL
56	$C_9H_{13}N_3OS$	LIQUID
57	$2(C_9H_{14}N_3OS)C_2O_4$	TAN SOLID
58	$C_{11}H_{17}N_3OS$	OIL
60	$C_{12}H_{19}N_3OS$	DARK OIL
62	$C_{14}H_{23}N_3OS$	SOLID
63	$C_{14}H_{14}FN_3OS$	DARK OIL
64	$C_{11}H_{15}N_3OS$	OIL
65	$2(C_{11}H_{16}N_3OS)C_2O_4$	132-134 °C
66	$C_{11}H_{13}N_3OS$	LIQUID
67	$C_{12}H_{15}N_3OS$	OIL
68	$C_{12}H_{15}N_3OS$	OIL
71	$C_{11}H_{17}N_3S_2$	OIL

Compound No.	Empirical Formula	Melting Point/Physical State
72	$C_{12}H_{19}N_3S_2$	DARK OIL
73	$C_{13}H_{21}N_3S_2$	OIL
74	$C_{14}H_{20}N_4S_2$	DARK OIL
75	$C_{14}H_{23}N_3S_2$	OIL
77	$C_{11}H_{15}N_3S_2$	DARK OIL
79	$C_{13}H_{19}N_3O_2S$	OIL
100	$C_9H_{13}N_3S$	OIL
102	$C_9H_{12}ClN_3S$	OIL
103	$C_9H_{11}Cl_2N_3S$	93-95 °C
104	$(C_9H_{12}Cl_2N_3S)Cl$	93-95 °C
107	$C_{10}H_{15}N_3OS$	OIL
108	$C_{11}H_{17}N_3OS$	OIL
109	$C_{12}H_{19}N_3OS$	OIL
110	$C_{13}H_{21}N_3OS$	OIL
111	$C_{15}H_{25}N_3OS$	OIL
130	$C_7H_4ClN_3S$	SOLID
131	$C_7H_4FN_3S$	LIGHT YELLOW OIL
132	$C_8H_7N_3S$	55-57 °C
140	$C_{10}H_{11}N_3OS$	OIL
141	$(C_{11}H_{14}N_3OS)I$	123-127 °C
145	$C_{10}H_9N_3OS$	55-57 °C
146	$(C_{11}H_{12}N_3OS)I$	131-134 °C
161	$(C_{10}H_9ClN_3O_2S)BF_4$	118-120 °C
162	$(C_{14}H_{11}ClN_3S)Br$	47-49 °C

Candidate pesticides, i.e., insecticides of the present invention were evaluated on 7-10 day old cotton seedlings infested with cotton aphid (*Aphis gossypii*). At least 12 hours prior to the test, leaf cuttings containing about 50 adult aphids were placed on leaves of each of duplicate cotton seedlings for each rate of application of candidate insecticide. Solutions of the candidate insecticide were prepared for testing by serial dilution of a standard solution comprised of an appropriate amount of insecticide in a water/acetone solvent, which contained a small amount of a surfactant. Rates of application of candidate insecticide may range from about 1000 ppm, or more, to about 3 ppm, or less, in a rate series of, for example, 1000 ppm, 100 ppm, 30 ppm, 10 ppm, and 3 ppm. The solutions containing each rate of application of candidate insecticide were then sprayed to run-off to both the upper and lower portions of the leaves of the aphid-infested cotton seedlings. Each test of foliar-applied candidate insecticide included appropriate standard insecticide of known insecticidal activity and blank treatments to aid in assessing the insecticidal activity of the candidate insecticide. Upon completion of the spraying with

candidate insecticide, the cotton seedlings were maintained in a growth chamber for a period of 72 hours. After this time, the seedlings were examined for dead insects. Insects were classified as dead if they were off-color or brown and desiccated. Upon completion of the evaluation of the test, the percent mortality of the cotton aphid for each rate of application of the candidate insecticide was determined by comparison of the total number of dead insects to the total number of insects in the test. Table 3 sets forth the insecticidal activity of the compounds tested in this test.

Table 3
Insecticidal Activity of 1,2,5-Thiadiazoles
Foliar Tests against Cotton Aphids

Compound No.	Rate of Appln. (ppm)	Percent Mortality[1,2]
2	1000	LP
3	1000	LP
4	1000	86
	300	73
	100	24
23	1000[3]	11
57	1000[3]	19
60	1000	LP
63	1000[3]	48
68	1000	LP
71	1000[3]	23
73	1000	LP
75	1000	25
100	300	90
102	1000	33
	300	8
107	1000	24
	300	12
108	1000	17
	300	3
109	1000	67
	300	17
110	1000	LP
111	1000	25
	300	7
132	1000	82
	300	35
140	1000	LP

[1] Percent mortality is derived from the number of dead insects (TD) relative to the total number of insects (TI) used in the test,

% Mortality = TD/TI x 100

[2] LP means that some activity was observed because the population of the cotton aphids was lowered but a value was not calculated.
[3] Average of two tests.

Compounds of the present invention provided insecticidal activity in the foliar test against the cotton aphid. Four of the compounds set forth in Table 3 provided insect mortality of greater than 65% (Compounds 4, 100, 109 and 132), of which three of the compounds provided insect mortality of greater than 80% (Compounds 4, 100 and 132).

Candidate pesticides, i.e., acaricides of the present invention were evaluated on 7-8 day old pinto bean seedlings infested with two-spotted spider mite (*Tetranychus urticae*) in comparison with the corresponding 1,2,4-thiadiazole derivatives. The test was conducted using the test method set forth below:

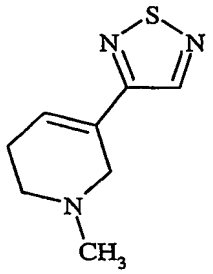
One to two hours prior to the test, leaf cuttings containing about 50-75 adult mites were placed on leaves of each of duplicate pinto bean seedlings for each rate of application of candidate acaricide. Solutions of the candidate acaricide were prepared for testing by serial dilution of a standard solution comprised of an appropriate amount of acaricide in a water/acetone solvent, which contained a small amount of a surfactant. Rates of application of candidate acaricide may range from about 1000 ppm, or more, to about 1 ppm, or less, in a rate series of, for example, 1000 ppm, 300 ppm, 100 ppm, 30 ppm, 10 ppm, 3 ppm, and 1 ppm. The solutions containing each rate of application of candidate acaricide were then sprayed to run-off to both the upper and lower portions of the leaves of the mite-infested pinto bean seedlings. Each test of foliar-applied candidate acaricide included appropriate standard acaricide of known acaricidal activity and blank treatments to aid in assessing the acaricidal activity of the candidate acaricide. Upon completion of the spraying with candidate acaricide, the pinto bean seedlings were maintained in a growth chamber for a period of 72 hours. After this time, the seedlings were examined for dead acarids. Acarids were classified as dead if they failed to show movement when probed. Upon completion of the evaluation of the test, the percent control of the two-spotted spider mite for each rate of application of the candidate acaricide was determined by comparison of the total number of dead and motibund

acarids to the total number of acarids in the test. Table 4 sets forth the acaricidal activity of the compounds tested in this test.

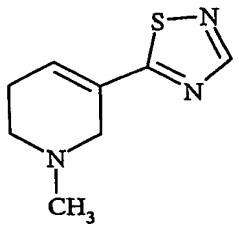
Table 4
Acaricidal Activity of 1,2,5-Thiadiazoles in Foliar Tests against Two-Spotted Spider Mites; A Comparison With Corresponding 1,2,4-Thiadiazoles

Compound Number	Rate of Application (ppm)	Percent Control
4	1000	100
	300	100
	100	100
	30	96
	10	49
23	300	100
	100	98
	30	95
	10	35
57	1000	53
	300	34
58	1000	56
	300	27
60	1000	41
	300	10
66	1000	98
	300	83
	100	52
67	1000	100
	300	100
71	1000	69
	300	20
72	1000	34
	300	4
77	1000	92
	300	13
102	1000	77
	300	27
	100	13
109	1000	65
	300	15
110	1000	87
	300	34
A	300	Inactive

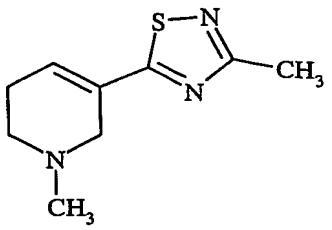
Compound Number	Rate of Application (ppm)	Percent Control
B	300	Inactive



Compound 4
a 1,2,5-thiadiazole



Compound A
a 1,2,4-thiadiazole



Compound B
a 1,2,4-thiadiazole

[1] Percent mortality is derived from the number of dead acarids (TD) plus the number of moribund acarids (TM) relative to the number of acarids (TI) used in the test,

$$\% \text{ Control} = (TD + TM)/TI \times 100$$

Compounds of the present invention showed unexpectedly improved activity in the foliar test against the two-spotted spider mite when compared to the corresponding 1,2,4-thiadiazole derivatives. At a low application rate of 300 ppm, compounds 4, 23, 66 and 67 all provided better than 80% control of two-spotted spider mite, with compounds 4, 23, and 67 providing 100% control. In contrast, compounds A and B, the 1,2,4-thiadiazole derivatives, were completely inactive at the application rate of 300 ppm. At the higher rate of application of 1000 ppm, compounds 57, 58, 60, 71, 72, 77, 102, 109 and 110 provided control of two-spotted spider mite varying from 34% to 92%.

While the invention has been described in detail and with reference to specific embodiments thereof, it will be apparent to one skilled in the art that various changes and modifications can be made therein without departing from the spirit and scope of the invention as defined by the following claims.